EPIDEMIOLOGICAL AND CLINICAL PROFILE OF HUMAN LEPTOSPIROSIS IN NORTH CHENNAI – A STUDY OF 90 CASES

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. BRANCH - I

GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA

MARCH 2008

CERTIFICATE

This is to certify that the dissertation titled **"EPIDEMIOLOGICAL AND CLINICAL PROFILE OF HUMAN LEPTOSPIROSIS IN NORTH CHENNAI – A STUDY OF 90 CASES"** is the bonafide original work of **DR.N.LOGANATHAN** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2008. The Period of study was from February 2006 and May 2007.

PROF S.NATARAJAN, M.D., Professor and Head Department of Medicine Govt. Stanley Medical College and Hospital Chennai 600 001	**PROF S.SHIVAKUMAR, M.D.,** Professor of Therapeutics Govt. Stanley Medical College and Hospital Chennai 600 001

Dr. MYTHILI BHASKARAN, M.D.,
D E A N
Govt. Stanley Medical College and Hospital
Chennai – 600 001

DECLARATION

I, **DR.N.LOGANATHAN,** solemnly declare that dissertation titled **"EPIDEMIOLOGICAL AND CLINICAL PROFILE OF HUMAN LEPTOSPIROSIS IN NORTH CHENNAI – A STUDY OF 90 CASES"** is a bonafide work done by me at Government Stanley Medical College and Hospital during February 2006 to May 2007 under the guidance and supervision of my unit chief **Prof. S.SHIVAKUMAR, M.D.,** Professor of Therapeutics, Government Stanley Medical College and Hospital, Chennai.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine – March 2008.**

Place : Chennai.

Date : 26.11.2007

(DR. N. LOGANATHAN)

ACKNOWLEDGEMENT

I owe my thanks to the Dean, Govt. Stanley Medical College and Hospital, **Dr. MYTHILI BHASKARAN, M.D.,** for allowing me to avail the facilities needed for my dissertation work.

I am grateful to **Prof. S. NATARAJAN, M.D.,** Professor and Head of the Department of Medicine, Govt. Stanley Medical College and Hospital for Permitting me to do the study and for his encouragement.

I express my gratitude to **Prof. S. SHIVAKUMAR, M.D.,** Professor of Therapeutics, Chief of Medical Unit II, Government Stanley Medical College & Hospital for his valuable assistance and guidance.

I am extremely thankful to **Dr. K.H. NOORUL AMEEN, M.D.,** Medical Registrar and to my Assistant Professors **Dr. C. SUKUMAR, M.D.,** and **Dr. T. ARUN, M.D.,** for their guidance and encouragement.

I am also thankful to my colleagues for their full cooperation in this study and my sincere thanks to all the patients who co-operated for this study.

CONTENTS

INTRODUCTION

INTRODUCTION

Infectious disease is an important cause of morbidity and mortality in our country. Leptospirosis is one of the most widespread zoonotic infection in world today and it has long been considered a rare zoonotic disease in India with only sporadic cases being reported[1,2].The disease has been reported from various States during the monsoon months in mini epidemic proportions.Cases have been reported from Kerala, Tamil Nadu, Gujarat, Andamans & Nicobar islands, Karnataka, Maharashtra, Orissa,Puducherry and in other states like Uttar Pradesh and Andhra Pradesh[3,4].

Leptospirosis has been under reported and under diagnosed from India due to a lack of awareness of the disease and lack of appropriate laboratory diagnostic facilities in most parts of the country. Combining clinical expertise and awareness with rapid tests for diagnosis will increase the recognition of patients with leptospirosis.Leptospirosis can be diagnosed only by laboratory tests, as the clinical features are non-specific.

Recently, the diagnosis of leptospirosis has been simplified by utilizing the Modified Faine's Criteria[5]. This study has been undertaken to study the epidemiological profile and clinical profile of leptospirosis in our hospital, which caters to the population in North Chennai.

AIM OF THE STUDY

AIM OF THE STUDY

1. To evaluate the epidemiological risk factors for leptospirosis.
2. To study the clinical profile leptospirosis utilizing Modified Faine's Criteria in North Chennai.

REVIEW OF THE LITERATURE

REVIEW OF THE LITERATURE

HISTORY

In 1886, Weil described a severe icteric disease which appeared to be a unique clinical illness. Inada et al cultivated the casual agent, a spirochete in 1915 and called this organism 'spirochete Icterohemorrhagiae[6]. Shortly after the identification of leptospira, icterohemorrhagiae in man, the significance of the rodent as a vector and reservoir of icterohemorrhagiae became apparent.

MICROBIOLOGY

The genus leptospira comprises the pathogenic leptospires (L. interrogans) and the saprophytic leptospires (L. biflexa). L. interrogans comprise 23 serogroups and over 200 serotypes. Leptospires have a narrow diameter of 0.1μm and vary in length from 3μm to 20μm. It ends are hooked. It has both primary and secondary coils. They are very actively motile and because of unique motility and narrow diameter, flexibility and shape allow leptospires to pass through even 0.1 – 0.45μm pore diameter membrane filters.

Surrounding the leptospiral cell is 3 – 5 layered membrane, the outer envelope. It encloses protoplasmic cellular components.Two flagella are located between the outer envelope and protoplasmic cylinder one at each end of the cell.The cytoplasm contains nuclear material, ribosomes, mesosomes and inclusion bodies.

THE ECOLOGY OF HUMAN LEPTOSPIROSIS

Leptospirosis is a disease characterized by broad spectrum of clinical findings caused by a single family of organisms of which there are multiple serogroups and serotypes. The disease reflects the sociological history of the nation, movement of its population from rural to an urban environment,the occupations of its inhabitants and the leisure time activities of the populace[6].

EPIDEMIOLOGY

Rodents, domestic & wild animals form the reservoir of infection where domestic animals such as cattle, dogs, pigs may act as carriers for several months (temporary carriers) while rodents usually remain as carriers throughout their life (permanent carriers). Thus rodents are considered the major reservoir of infections. Leptospires are excreted in the urine of the animals and they affect human being when they come into contact with the urine of infected animals, directly or indirectly, when exposed to an environment contaminated by the urine of the infected animals such as soil and surface water following monsoon rains. Therefore, the illness occurs commonly during the monsoon months. The infection is probably transmitted when they wade through stagnant rainwater contaminated by the infected urine of animals.These organisms survive for six hours in dry soil and for six months in flooded conditions. They enter the host

through abrasions of the skin of the feet or intact mucous membranes of eye, throat and gut[7].

Leptospirosis can occur in both urban and rural areas. In urban areas of developing countries, a contaminated environment due to various factors such as over crowded slums, inadequate drainage and sanitation facilities for both man and animals, presence of stray dogs, cattle, pigs, domestic rats, bandicoots, poor condition of slaughter houses and people walking bare foot contribute to the spread of the illness[8,9].

In rural areas, high-risk groups are workers in rice fields, cane fields and other agricultural crops and animal husbandry staff. In addition, the workers in sewers, mines and military personnel are also at risk. It is impossible to trace the source of infection and any person can be infected, irrespective of direct contact with animals, due to the contaminated environment. Therefore, the more important epidemiological factors are rainfall, contact with contaminated environment and animal's contact. The number of cases in a region often fluctuates from year to year due to various factors such as rainfall, flooding and animal infections.

ANIMAL RESERVOIRS

Leptospirosis is one of the widespread zoonosis. Mammals are the most important animal reservoirs. Leptospires are parasites of both wild and domestic animals. A wide variety of animals may serve as a source of infections like rats,

fox, mongoose, field mice, hedgehog and domestic animals like cattle, sheep, goats and poultry. Epidemiological role of non-mammalian hosts such as reptiles and birds is not well understood. In infected animals, initial leptospiremic phase is followed by a period, in which the organism is confined to kidneys. Leptospires are excreted in the urine and the animal is a carrier.

It is now known that a particular host species may serve as reservoir for one or more serotypes of leptospires and conversely a given serotype may be hosted by multiple animal species. The seovars most frequently associated with rodents are icterohemorrhagiae and autumnalis, with cattle pomona, harchijo and grippotyphosa, with swine pomona and tarhassori, with sheep and goats pomona and grippotyphosa, with horses pomona and with dogs canicola and icterohemorrhagiae. Man is an accidental host, the carrier state is transient and in maintenance host it may be present for many years[10].

INFECTIONS BETWEEN FARM ANIMALS

There are two means of transmission. The first is by a congenital or neonatal infection followed by recovery and continuing carrier state. The second is spread from the urine of carriers onto farmyard floors (or) sources of drinking water.

INFECTIONS BETWEEN FARM ANIMALS AND RODENTS

Rodents especially cats may infect both farm animals and their own species. This is a common cycle for infection of cattle and pigs.

INFECTIONS BETWEEN FARM ANIMALS, WATER AND RODENTS

The rodent carriers contaminate water or soil which then becomes the source of infection for pigs, cattle or sheeps which in turn become carriers and execretors, thus infecting other rodents or more of their own species. The contaminated water is a potential source of infection for man. This is the common epizootiological – epidemiological pattern in the rice-growing parts of the world.

INTERACTION WITH FERAL RODENTS

The intrusion of man into feral rodents habitats involves him the risk of acquiring leptospirosis. Domestic animals intruding into the uncultivated habitats run similar risk. Conversely the incursions of foraging feral animals into populated areas pose risks for both people and farm animals[7].

TRANSMISSION TO HUMAN HOST

The transmission of leptospiral infection from animals to man occurs directly by contact with blood, tissues, organs and urine of infected animals or indirectly (more commonly) by exposure to an environment contaminated by leptospires (water and soil contaminated by infected urine). Human to human transmission rare.

ENTRY

The leptospires enter through cuts and abrasions in the skin or mucus membrane such as conjunctiva, vagina, nasopharynx and intestine. The leptospires do not cause local inflammatory reaction.

ENVIRONMENT

Transmission of leptospires depends not only on the relationship between animal reservoirs and man, but also on the environment which favours survival of leptospires outside the animal host.

Optimal factors for survival of leptospires are the presence of moisture, warmth (28 – 32^{o}C), pH values of soil and surface water (6.2 – 8). Factors which impede survival are salinity, chemical pollution and acidic pH. Flooding after heavy rains is favourable for leptospires and it can survive for a few hours in dry soil but can survive for six months in flooded conditions[10].

ENVIRONMENTAL CONTAMINATION

In urban and rural areas of developing countries where leptospires are widespread in the environment and endemic, the infection is related to "the way of life" as well as to the specific occupations. Thus where there are large numbers of rodents, stray dogs and wild animals, where people drink or bathe in untreated water where sewerage and drainage are inadequate, where garbage disposal is

inefficient and open shoes or none at all are worn, leptospiral infection can be common. This was pointed out by Everard and Everard[8].

Fresh water was recognized as an important vehicle for the transmission of leptospiral infections to man. Rat urine contamination of water in wells, sewers, etc., remains an important mode for the transmission of leptospirosis to man. Surface waters into which organisms are excreted may remain infectious for several weeks[6].

In Barbados, 97% of human hospital cases are caused by L. bimo, L. copenhageni and L. arborae, all of which are mainly maintained by rodents on the island. In England and Wales between the year 1985 – 89, the average annual number of confirmed cases was 60, 12/100000 per year. The minimum incidence of severe illness in Dominica between 1989 – 90 (23/100000) was 192 times higher than that of England and Wales implicating environmental contamination[9].

In another study from Chennai, there has been dramatic increase in leptospirosis during the past few years between the year 1979 – 84, there were only 9 cases of leptospirosis in the Government General Hospital, Chennai, while between1987 – 93 there were 176 cases[11] (shown in Table 1).

Table 1 : Annual incidence of leptospirosis

Year	1987	1988	1989	1990	1991	1992	1993	Total
Leptospirosis	4	21	26	60	48	8	9	176

OCCUPATIONAL RISK FACTORS

In most areas of the world, leptospirosis is primarily an occupational disease. Agricultural workers have the highest risk of infection, but persons who work in other rodent infested environment are also at risk of infection. Other occupations related to risk are conservancy workers, abattoirs, hunters, fishermen, garbage cleaners, veternarians and laboratory workers and livestock handlers[10].

1. AGRICULTURE

The raising of 'wet' land crops such as rice is hazardous as workers often work with their bare feet and hands immersed in water for prolonged periods of time. The persons involved in raising 'dry' land crops such as sugarcane, vegetables and various grains are exposed to the risk of infection, which is greatest during harvesting.

Major epidemics can occur when seedlings are transplanted into flooded fields by farmers who work for long periods bare footed and have handed and when crops that are particularly vulnerable to attack by rodents are harvested. Wet soil and heavy early morning dew, mixed with urine voided at night by nocturnal rodents or infected livestock in pastures poses a threat to early morning field workers, particularly in the tropics. Cutting and handling of crops like sugarcane and pineapples frequently cause skin abrasions which may increase possibility of infections.

In one survey in the Caribbean region found, that 45% sugarcane farmers, 33% rice workers, 36% of vegetable and fruit farmers and 20% of animal handlers had been exposed to the disease[7].

2. LIVESTOCK

Persons who raise livestock may be infected from exposure to their, animal's urine either directly or indirectly. Infection may also occur from helping an infected animal to give birth or while cutting up infected dead animals.

3. Leptospirosis is also an occupational disease among workers in poultry, fish processing plants and slaughter houses. Poultry and fish are not infectious but infestation of processing plants with rodents leads to contamination of the working area. Rodent infestation of slaughter houses will also increase the rate of infection.

4. Miners, conservancy staff (sewer workers, garbage cleaners), construction workers, military personnel, hunters and fishermen are workers at risk of infection. Veternarians and laboratory workers are also at risk[10].

A study done by Heath, Alexander and Galton of 483 cases of human leptospirosis reported in United States between 1947 – 60 emphasized the importance of occupation to the risk of acquiring the infection. The probable infecting source was ascertained in 191 cases. 31% involved contact with rats, while 30% were associated with dog exposure, in 20% cattle were implicated as the source of infection[12].

The possible infecting serotype was established by Heath in 409 of 481 cases by serological studies. The commonly encountered serotypes were icterohemorrhagiae-41 %, canicola-28 %, pomona-20 %. Majority of infections due to icterohemorrhagiae could be traced to rat exposure either directly or indirectly through water immersion. Canicola related cases were linked to dog contact, while majority of pomona infections were associated with cattle and swine exposure. In the majority of cases collected by Heath, infection was acquired during the summer and early fall months (63% during June to September).

In another study from Kottayam (Kerala), about 900 cases of fever, jaundice, renal failure over a period of 10 years, the following data were noted. About 50% of patients were in the age group of 29 – 39 years and male/female ratio was 7%. About 74% of the cases occurred during the rainy season from June to November. Disease was commonly seen in agricultural workers, fishermen and oyster shell catchers. Because of heavy rat infestations in many households, even students, officers and housewives were affected by the illness[13].

In a study from Chennai, the maleness, high rainfall and outdoor manual occupation (Table 2) encourage higher incidence rates of leptospirosis. The patients came from various parts of the city and no geographical clustering of cases was evident[8].

TABLE 2: Occupations of 57 cases of leptospirosis in Madras city

Work Category	Number	Percentage
Outdoor manual workers	28	49
Indoor/outdoor artisans	7	12.3
Outdoor non manual workers	5	8.8
Indoor non manual workers	6	10.5
Housewives	7	12.3
Unemployed	1	1.8
Retired	1	1.8
Unknown	2	3.5

RECREATIONAL EXPOSURE

The water located in rural areas, developed for recreational purposes provide a habitat for wild life and also are used as a water supply for livestock. Many outbreaks of human leptospirosis acquired by exposure to contaminated water have been described. In 1951, Shaeffee reported 50 cases of pomona infection among a group of 80 young people, which followed a swimming party in a creek located in a pasture for swine and cattle. It is likely that the natural water sources supplying the pool were contaminated by dog or deer or other animal urine[6].

A total of 140 cases of human leptospirosis were reported from 1947 – 64 in Iowa. Of these, 55 cases occurred in 2 outbreaks in 1959 – 64 as a result of swimming in water contaminated with leptospires. Galton et al summarized several other recent outbreaks of leptospirosis acquired by swimming in contaminated water sources. Importance of dogs in the transmission of leptospirosis to man was highlighted as a result of an investigation following an outbreak of leptospirosis in St.Louis, Missouri suburb in November 1972[6]. In one study from Hawaii, United States, it was found 43% of cases were exposed through recreational activities, including fresh water swimming, hiking, camping and hunting[14].

RAINFALL

Rainfall is one of the important epidemiological risk factors of spread of leptospirosis. Flooding after heavy tropical rains elevates the water table, allowing saturation of the environment by subsurface leptospires. It prevents animal urine from evaporating or penetrating the soil so that leptospires may pass directly into the surface waters and tops up swampy zones, causing invasion by aquatic rodent or carnivore population from neighbouring cultivated fields. Large outbreaks typically involve a group of people, who have been immersed in floods.

Between November 1979 and the end of December 1986 (7.17 yrs), 248 cases of leptospirosis were confirmed among hospital patients in Barbados (mean age:35) and considering the 235 who were $\geq$ 15 years of age, the annual incidence

of leptospirosis was 19.2/lakh population. There were 173 males and 62 females. The incidence in areas with rainfall > 1800 mm (32.6/lakh) was nearly that in areas without rainfall < 1600 mm (17.3/lakh). There is a link between cases of severe disease and recent rainfall. Rainfall is one seasonal factor known to influence the numbers of cases on Barbados as in other parts of the world[15].

Chennai is an important coastal metropolis in South India and has a land area of 172 km^2. The population is estimated to be about 5.3 million. The weather is warm and humid, with an average yearly rainfall of about 1500 mm. Most of the rainfall comes with the North East monsoon (October – December). In Chennai City, between 1979 – 84, there were only 9 cases of leptospirosis in the Government General Hospital, Chennai while between 1987 – 93, there is an increase of cases to 176 cases[11] as shown in Table-1. Most cases occurred in monsoon months as shown in Table-3. The infection is probably transmitted to people when they wade through stagnant rainwater contaminated by infected urine of animals. This emphasizes the epidemiological importance of a contaminated environment in the spread of leptospirosis.

Table: 3 Monthly incidence of leptospirosis (1987 – 1993)

January	February	July	September	November	December	Total
5	1	1	4	100	65	176

Figure 1: Shows the barefoot walking in the contaminated environment after the rainfall.

Figure:1

SERO SURVEY

Sero survey is an important epidemiological tool for assessing the burden of infection in the community. A serosurvey for leptospiral antibodies was made in 1375 persons in Northern Trinidad between the years mid 1977 – 78. Subjects were employees in seven occupational risk groups and three rural and urban communities from general population. High prevalence was found in sugarcane workers – 45%, rural village – 37% and 5% - wood brook, keeping cattle, walking bare foot and hunting was associated with significant leptospiral serology[16].

INDIAN STUDIES

Leptospirosis has long been considered a rare zoonotic disease in India with only sporadic cases being recorded[1,2]. Since 1980's the disease has been reported from various states during monsoon months in mini epidemic

proportions. The disease is endemic in Kerala Tamilnadu, Gujarat, Andamans, Karnataka, Maharashtra.It has also been reported from Andhra Pradesh, Orissa, West Bengal, Uttar Pradesh, Delhi & Puducherry[3,4].

The disease is endemic in south Gujarat since 1994[3,17,18].Leptospirosis has been reported regularly since 1998 in Maharashtra[3,19,20]. The incidence of leptospirosis & deaths due to it in Gujarat[3,21] and Maharashtra is given in the table 4.

Table:4 Incidence of leptospirosis in Gujarat and Maharashtra

Year	Gujarat		Maharashtra	
	No	Death	No	Death
2003	373	40	350	24
2004	630	92	225	18
2005	392	81	2355	167

In a study of leptospirosis from kottayam (Kerala) of 900 cases treated over 10 years,Jaundice- (80 %), renal failure (59 %), hypotension (20 %) were the common complications noted. The disease was commonly seen in agricultural workers, fishermen and oyster shell catchers (82 %). 74 % were seen during the monsoon months with a male / female ratio 7:1[13]

Andaman and Nicobar Islands are endemic for leptospirosis since early part of the 20 th century. Outbreaks of Andaman Haemorrhagic fever (AHF) were reported since 1988. This was proved to be leptospirosis in 1994. 524 cases of AHF (leptospirosis) were reported from 1988- 97[3,22,23]. The disease presented as febrile illness with pulmonary haemorrhage during post monsoon periods. As the disease presented with predominant pulmonary involvement, a leptospiral etiology was never

considered. In addition, absences of diagnostic facilities were responsible for not diagnosing leptospirosis [22].

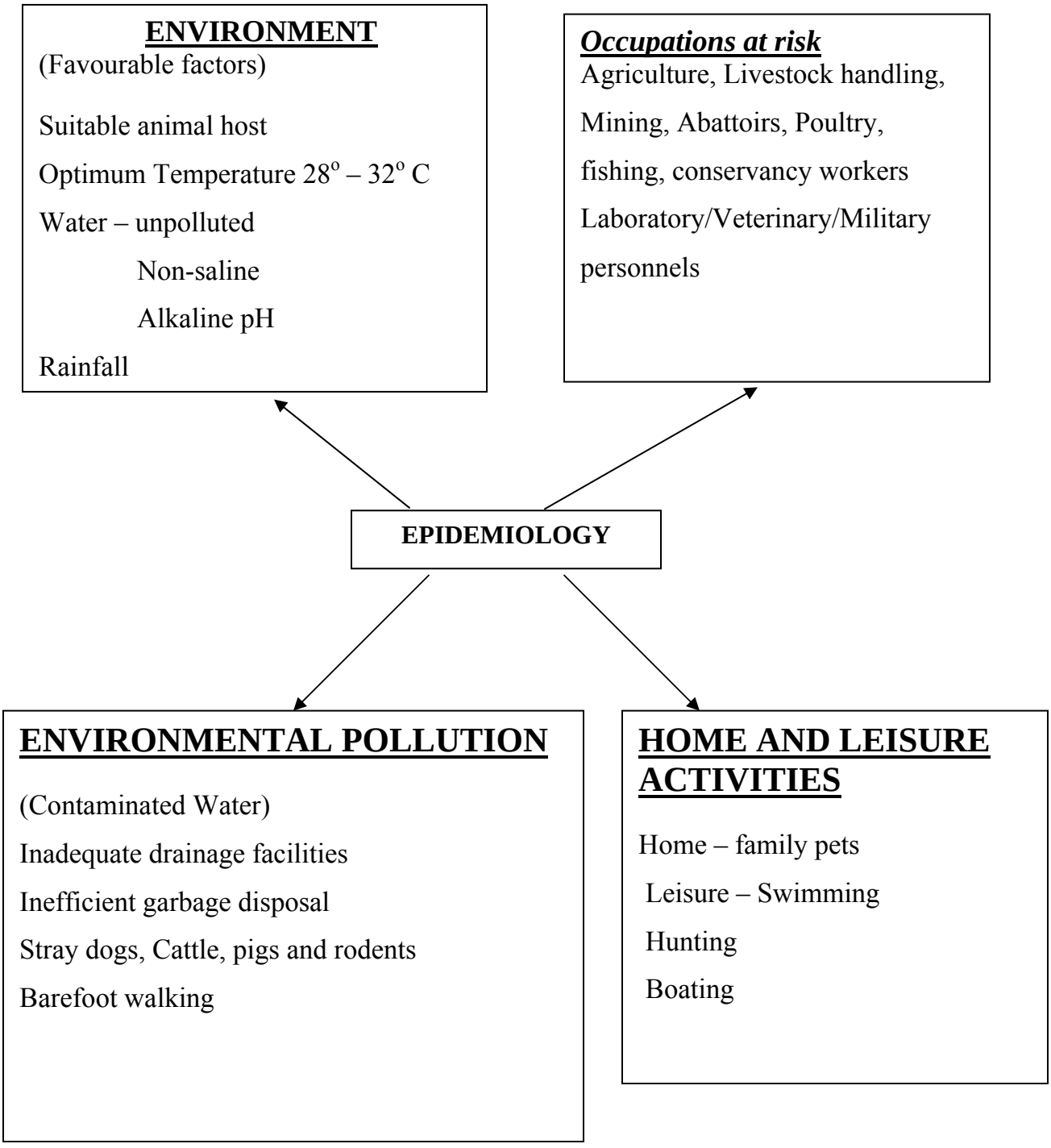
In Chennai, during the period 1987 – 91 , there were 159 cases of leptospirosis at the General Hospital, Chennai (Table 1). There were 108 males and the mean age was 40.1 years. 136 (85%) patients had jaundice and 120 (75%) patients had renal failure. 70 patients were dialyzed and 25 patients died (15.6 %)[24].

In the recent past, acute renal failure due to leptospirosis at General Hospital, Chennai has significantly declined from 31 % in 1987 – 91 to 7.5 % in 1995-2004[25]. Of the 120 cases of leptospiral ARF during the period 1987-91,the highest number of 45 cases were reported in 1990. Since 1992 there has been a decline in leptospiral renal failure cases and during a 10 year period from 1995 -2004 only 84 cases were reported[26].

In a recent study of 106 cases of leptospirosis from north Chennai, jaundice occurred in 17.8 % and renal failure occurred in 10.3 % showing a decline in complications. Only two patients were dialyzed and there were no deaths. Fever, headache, myalgia were the common presentations. Contaminated environment (95 %) and rainfall (50 %) were the important epidemiological risk factors. Icterohaemorrhagiae was the most common serogroup detected[26].

The interrelationship between environmental contamination, high risk occupations and home and leisure activities is shown in table:5.

Table:5


ENVIRONMENT
(Favourable factors)
Suitable animal host
Optimum Temperature 28° – 32° C
Water – unpolluted
Non-saline
Alkaline pH
Rainfall
Occupations at risk
Agriculture, Livestock handling,
Mining, Abattoirs, Poultry,
fishing, conservancy workers
Laboratory/Veterinary/Military
personnels
EPIDEMIOLOGY
ENVIRONMENTAL POLLUTION
(Contaminated Water)
Inadequate drainage facilities
Inefficient garbage disposal
Stray dogs, Cattle, pigs and rodents
Barefoot walking
HOME AND LEISURE ACTIVITIES
Home – family pets
Leisure – Swimming
Hunting
Boating

PATHOGENESIS

Once the organism gains entry, leptospires spread through the blood stream to all organs. Virulent organisms multiply in blood stream in a day or two. Agglutinating antibodies start appearing in the blood around 4th day. The organism is removed by reticuloendothelial system. These antibodies are detected by MSAT (Macroscopic slide agglutination test) and MAT (Microscopic Slide Agglutination test). After 4-7 days the organisms persist in the aqueous humor and in the renal tubules and are excreted in the urine for about 1-4 weeks.

Mechanism:

Direct effect – Extensive endothelial injury resulting in multiple hemorrhages, transudation of fluid from the vascular compartment and hypovolemia.

Kidney – It penetrates glomeruli,peritubular capillaries, interstitium , tubular lumen, ultimately leading to acute tubular necrosis and acute interstitial nephritis.

Liver- It produces hepatocellular necrosis , cholestasis

Immunological reaction- meningitis and uveitis in leptospirosis are the result of immunological injury.

Non-specific factors- Hypovolemia, hypoxemia, hyperviscosity, DIC, intravascular hemolysis & myoglobinuria. All these factors contribute to widespread disturbance in microcirculation[10].

CLINICAL FEATURES

The clinical features of leptospirosis are varied with mild anicteric illness to severe illness.

Mild → Fever, myalgia, conjunctival suffusion

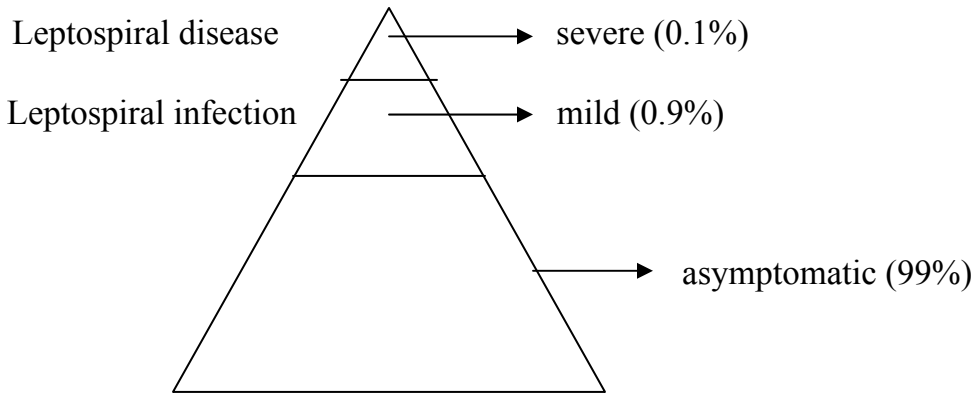
Severe→ Jaundice, meningitis, renal failure.

The incubation period ranges from 2 – 21 days. 90% of cases are anicteric. The usual course of illness is biphasic consisting of leptospiremic phase and immune phase[10].

Clinical spectrum of leptospirosis

Most of the leptospiral illness is asymptomatic constituting around 99%. Mild leptospiral illness constitutes 0.9 % and severe illness constitutes around 0.1% (shown in table 6).

Table: 6 Clinical spectrum of leptospirosis



Incidence: 10 – 100 / 100,000 population per year

Prevalence: 20 – 50%

The probable reasons for the disparity between incidence and prevalence is due to the circulation of pathogenic serovars for limited period in specific areas. The persistence of cases in endemic areas are due to the exposure of animals and humans to infection and development of protective antibodies. The development of severe infection may be related to immunological reasons.

ANICTERIC LEPTOSPIROSIS

This can be mild with fever, headache and body pain. Body pain is severe and most marked in lower limbs especially thighs and calves, severe pain in back, neck, abdomen and upper limbs are frequent. Anorexia, vomiting is frequent. The most characteristic finding on examination is conjunctival suffusion and severe myalgia. Leptospiremic phase subsides in 4 – 7 days. The immune phase is characterized by severe headache due to meningeal involvement, uveitis and low-grade fever. This lasts for 4 to 30 days or longer[10].

ICTERIC LEPTOSPIROSIS

In some patients, the septicaemic phase, progresses to a severe icteric illness with renal failure. Meningeal symptoms are frequent, but are overshadowed by hepatic or renal feature. Severe bleeding, hypotension, cardiac and pulmonary complications are frequent. Death occurs usually due to renal failure. Sudden death may occur due to massive bleeding, arrhythmias or Cardiac and respiratory failure[10].

KIDNEYS

Renal involvement is the most serious complication and is the commonest cause of death. Urinary sediment changes (Pyuria, hematuria and granular casts), to severe renal failure. Renal failure occurs in the 2nd week, but it can occur as early as the 4th day. It may be short lived or prolonged for up to two weeks. Renal failure can be due to pre renal component, acute interstitial nephritis and acute tubular necrosis[10].

LIVER

Jaundice is the most important clinical features of the severity of illness. Jaundice occurs between the 4th to 6th days of illness. Liver is often enlarged and tender. Marked elevation of serum bilirubin with mildly elevated transaminases is characteristic and is due to intra hepatic cholestasis. Death is rarely due to hepatic failure[10].

Fig 2 shows a patient with leptospiral hepatic dysfunction with jaundice.

Figure 2:

HAEMORRHAGIC FEVER WITH RENAL SYNDROME

Bleeding may occur from respiratory, alimentary renal and genital tracts occasionally into subarachnoid space and adrenals. This may be associated with renal failure and thrombocytopenia.

LUNGS (ATYPICAL PNEUMONIA SYNDROME)

Severe hemorrhagic pneumonitis may occur usually in the 2nd week. This can occur without jaundice (or) renal failure[10].

HEART

Cardiac complications are frequent in severe leptospirosis[27,28,29]. ECG changes ranging from low voltage complexes, non-specific ST, T wave changes, conduction defects and arrhythmias are seen. Atrial fibrillation is the most common arrhythmia observed. Severe manifestations such as cardiomegaly, cardiac failure and severe arrhythmias due to hemorrhagic myocarditis are observed. Sudden death may occur from cardiac failure or arrhythmias[30,31,32]. Patients can have cardiac complications secondary to hypokalemia. Hypokalemia is due to renal loss of potassium due to blockage of Na+ K+ ATPase pump in the ascending limb of loop of henle due to leptospiral proteins[33,34]. All cardiac abnormalities revert to normal within 2 to 3 weeks[10].

EYES

Conjunctival suffusion & haemorrhage is common in the septicemic phase and uveitis is common in the immune phase[10].

HYPOTENSION

It is due to hypovolemia secondary to vomiting, increased insensible water loss and diminished fluid intake, massive hemorrhage from gastro intestinal tract, vascular injury and myocardial dysfunction.

NERVOUS SYSTEM

This usually occurs in the immune phase and may present with signs of meningeal irritation. CSF shows lymphocytic pleocytosis, raised proteins and normal sugar.

LEPTOSPIROSIS DURING PREGNANCY

The hazards of leptospirosis during pregnancy include intrauterine infection with foetal death and abortion, stillbirths and premature labour. Leptospires may be secreted in the milk of lactating mothers especially during septicaemic phase[10].

In a study by Muthsethupathi M A, Shivakumar S et al from Chennai during 1990 – 1991 from Government General Hospital, Chennai, out of 70 patients with fever 57 cases of confirmed leptospirosis were seen[8] and the clinical features are shown in Table-7.

Of 57 cases of leptospirosis, 84% had jaundice and 72% had renal failure. All patients were febrile. Anicteric renal failure was 9.7%. Myalgia occurred in 82%, conjunctival suffusion in 58% and volume depletion in 39%. Thrombocytopenia occurred in 13 patients. 23 patients were dialyzed[8].

TABLE :7 Clinical features of leptospirosis (Chennai study – 1990-91)

Clinical Features	Chennai study (1990-91) n=57 %
Fever	100
Jaundice	84
Myalgia	82
Oliguria	72
Conjunctival suffusion	58
Vomiting	58
Altered sensorium	42
Volume depletion	39
Gastro intestinal bleed	26
Diarrhoea	26
Headache	26
Abdominal pain	18
Hemoptysis	9
Meningitis	7
Epistaxis	3

Leptospirosis constituted about 8% of acute febrile illness. In another study of 361 cases from Chennai by Shivakumar et al about clinical profile of infectious fevers the following data were obtained[35], as shown in Table-8.

TABLE : 8 Clinical profile of infectious fevers

Clinical Features	N=361 Frequency (%)
Tuberculosis	**51.3**
Pneumonia	**15.4**
Malaria	**12.8**
Leptospirosis	**8.2**
Enteric fever	**4.6**
Rheumatic fever	**2.6**
Liver abscess	**2.6**
Pyogenic meningitis	**2.6**
Infective Endocarditis	**1**

Leptospirosis constituted about 7.5% of acute renal failure. In a study from Government General Hospital, Chennai during the year 1995-04 of about 1112 patients of acute renal failure cases pointed out it[36]. This was less when compared to previous study in which leptospiral ARF was 31% in the year 1987 – 91[37]. This decline could be due to improved diagnostic facilities in diagnosing lot of anicteric cases and treating them aggressively to prevent complications. (Shown in Table 9).

TABLE:9 Etiology of ARF – chennai comparative data

Etiology	1987 – 91 n=387 (%)	1995 – 04 n=1112 (%)
Acute Diarrhoeal Disease	30.5	28.6
Leptospirosis	31	7.5
Drugs	5.4	13.4
Glomerulo nephritis	8.5	9.3
Snake bite	4.7	7.8
Copper sulphate poisoning	3.4	4.3
Malaria	--	4.4
Obstetric	3.4	8.9
Surgical	1.5	3.4

In another study from Chennai, by Muthusethupathi M A., Shivakumar S, et al 206 patients with leptospirosis were studied between 1987 – 1995[38]. The important clinical features noted were shown in Table 10.

Table:10 Clinical features of leptospirosis (Chennai study – 1987-1995)

Clinical Features	Percentage (%)
Fever	100
Jaundice	83
Renal Failure	79
Myalgia	79
Conjunctival suffusion	43
CNS dysfunction	43
Bleeding	28

In another comparative study the following data were noted (shown in Table 11). Fever, jaundice and renal failure were the important clinical features noted. The incidence of anicteric renal failure is low because lack of diagnostic facilities.

Table: 11 Clinical features – comparision of various studies

Clinical features	Barbados (Edwards et al)[39] % n = 88	United States (Heath et al)[12] % n = 345	Korea (Park et al)[40] % n = 93	Chennai (Muthusethupathi et al)[38] % n = 206
Fever	85	100	97	100
Renal Failure	49	26	15	79
Jaundice	95	43	16	83
Conjunctival suffusion	54	33	58	43
Myalgia	49	68	88	79
Bleeding Diathesis	2	4	40	-
CNS manifestations	2	21	6	43
Anicteric presentation	5	57	84	-

In Indian studies, the following clinical data were obtained. Jaundice and renal failure were the most important complications noted in Mumbai study of about 33% and 28%. Similar picture were also seen in Kottayam and previous Chennai studies. In Gujarat study conjunctival suffusion was common of about 58% and bleeding diathesis of about 34% (Shown in Table 12).

Table: 12 Indian studies – clinical features comparison

Clinical features	Mumbai Study[41] n = 74 %	Kerala (Kottayam)[13] n = 900 %	Gujarat (Surat)[1] n = 80 %	Chennai Study[38] n = 206 %
Fever	100	95	100	100
Headache	91.8	53	--	-
Myalgia	67.5	85	--	79
Conjunctival suffusion	35.1	65	58	43
Jaundice	33.7	80	--	83
Oliguria	28.3	59	46	79
CNS dysfunction	--	15	3.1	43
Cardiac	--	--	4	--

DIAGNOSIS OF LEPTOSPIROSIS

Laboratory support is needed:

1. To confirm the diagnosis
2. For epidemiological and public health reasons, to determine which serovar caused the infection, the likely source of infections, potential reservoir and its location.

The tests depend on the phase of infection. During leptospiremic phase (< 7 days) leptospires can be isolated by blood culture and PCR, while in the immune phase rising antibodies can be detected by serological tests[7,21].

Diagnostic Tests[10]

1. Microscopy
2. Culture
3. Animal inoculation
4. Serology

1. Microscopy:

Dark field Microscopy is required to see leptospires in the living state. They can be recognized in clinical specimens such as blood, urine and CSF as spiral organisms. Because of the artifacts confused with leptospires, microscopic examination is not recommended as a diagnostic procedure.

2. Culture:

The isolation of Leptospires by culture of blood, CSF and urine is the most definite way of confirming the diagnosis of leptospirosis. Culture of blood does not contribute to an early diagnosis as results come late, weeks or even months after inoculation in culture medium.

PCR is promising on both sensitivity and specificity, but is complicated and expensive.

3. Animal Inoculation:

Isolation may be attempted by inoculating the samples directly into the laboratory animals.

4. Serology:

The serological tests for diagnosis of leptospirosis have been classified as serovar specific tests and genus specific tests.

Serovar specific Tests:

Microscopic Agglutination Test (MAT):

MAT is the gold standard test for diagnosis of leptospirosis because of its unsurpassed diagnostic specificity. The main advantage is that serovars can be identified which is of epidemiological importance[14,21]. The difficulties in utilizing MAT are due to the following factors.

a. The antibody titers rise and peak only in 2nd or 3rd week, making it a less sensitive test.
b. The high titers of past infection persist for a long time (1 – 5 years) and therefore interfere with the diagnosis of current leptospirosis. Positive titers may represent a rising titer of current infection or declining titer of past infection.
c. The cut off titer for diagnosis of current infection depends on whether the area is endemic or non endemic, for example, the cut off titer varies from 1/80 to 1/400 according to various studies[21]. Therefore, a second sample is usually required. (to demonstrate a four fold rise in titer) to diagnose current infection. In endemic area titer of 1:400 is taken as high titer and in non-endemic areas 1:100 is taken as the diagnostic titer. Sero

epidemiological studies are required for determining the cut off value, as a single titer may not be adequate.

d. The test is complicated requiring dark field microscopy and cultures of various live serovars. This may not be available in small laboratories. Figure 3 shows the positive Microscopic Agglutination test (MAT) as seen under the dark ground microscopy.

Figure: 3. Positive MAT test:

Genus Specific Tests:

The two common tests are the ELISA and Macroscopic Slide Agglutination Test (MSAT). The other tests are latex agglutination test, complement fixation test and haemagglutination tests. The genus specific tests are the tests of choice for

the diagnosis of current infection. These tests are simple, more sensitive and become positive earlier than MAT[42].

These tests detect genus specific antibodies, which are shared by pathogenic and saprophytic leptospira. These tests become positive early in the disease (5- 6th day) as they detect specific IgM antibodies and help in rapid diagnosis of current infection[8].

ELISA: This is a popular test and can be performed with commercial kits or with antigen prepared "in house".

MSAT: The slide agglutination test is a simple macroscopic test in which a drop of the dense suspension of leptospira is mixed with a drop of serum on a slide and is examined by the naked eye for agglutination. If these tests are positive, they should be confirmed with MAT to identify the serovars. A 2+ agglutination titer is considered significant[42,43,44].

In a study from Brazil by Angelo Brendo et al noted that SAT seems to be a convenient test for the initial diagnosis of leptospirosis. It detected 65% of the cases of illness with admission sample and 94% with 2nd serum sample collected on about 17th day of symptom whereas, MAT showed only 40% positive rate by 1st sample. This shows that SAT is both sensitive and specific test[42].

In a study from the Institute of Microbiology, Madras Medical College, out of 592 samples received 317 samples were positive by IgM ELISA. Among these, MSAT was positive in 310 (sensitivity 97.8%). 303 samples had MAT titers of > 1:80. In all these patients, MSAT was positive. Autumnalis was the most

common serogroup (59.9%). 275 samples, which were negative by IgM ELISA, were also negative by MSAT. The MSAT has shown good correlation with both IgM ELISA and MAT[43] (shown in Table 13).

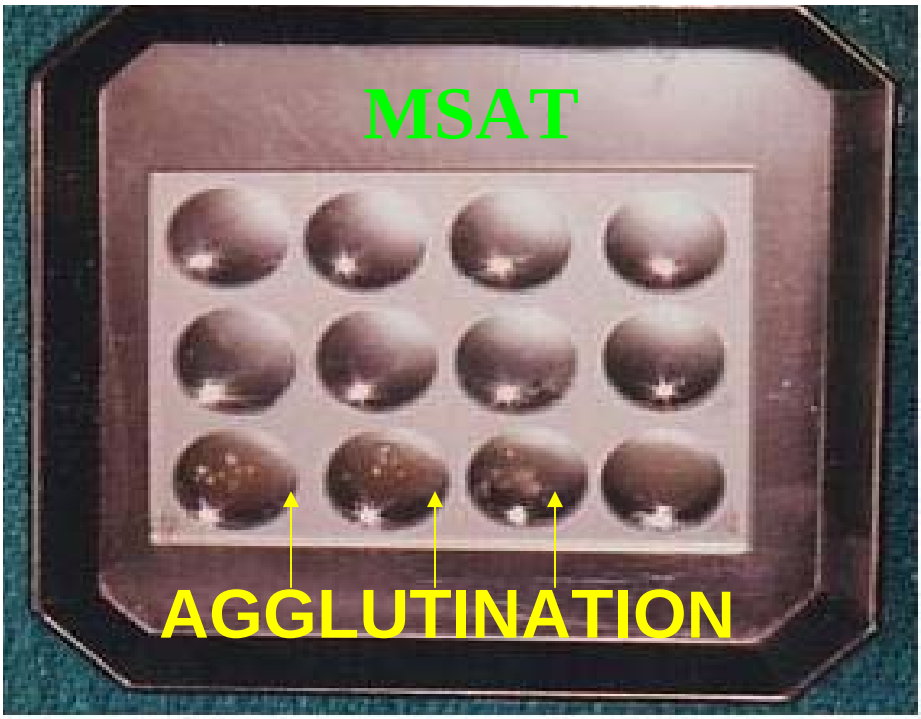
Table:13

Test Positive	**Patients N = 568**	**Samples N = 592**
IgM ELISA	293	317
MSAT	286	310
MAT (> 1:80)	279	303

Rapid slide Agglutination tests for leptospirosis are well established. Galton et al used 9 cultures and divided them into 3 groups (pooled 3 antigens in each group)[7] and found MSAT to be a sensitive test.

Figure 4 shows the positive Macroscopic Slide Agglutination Test (MSAT).

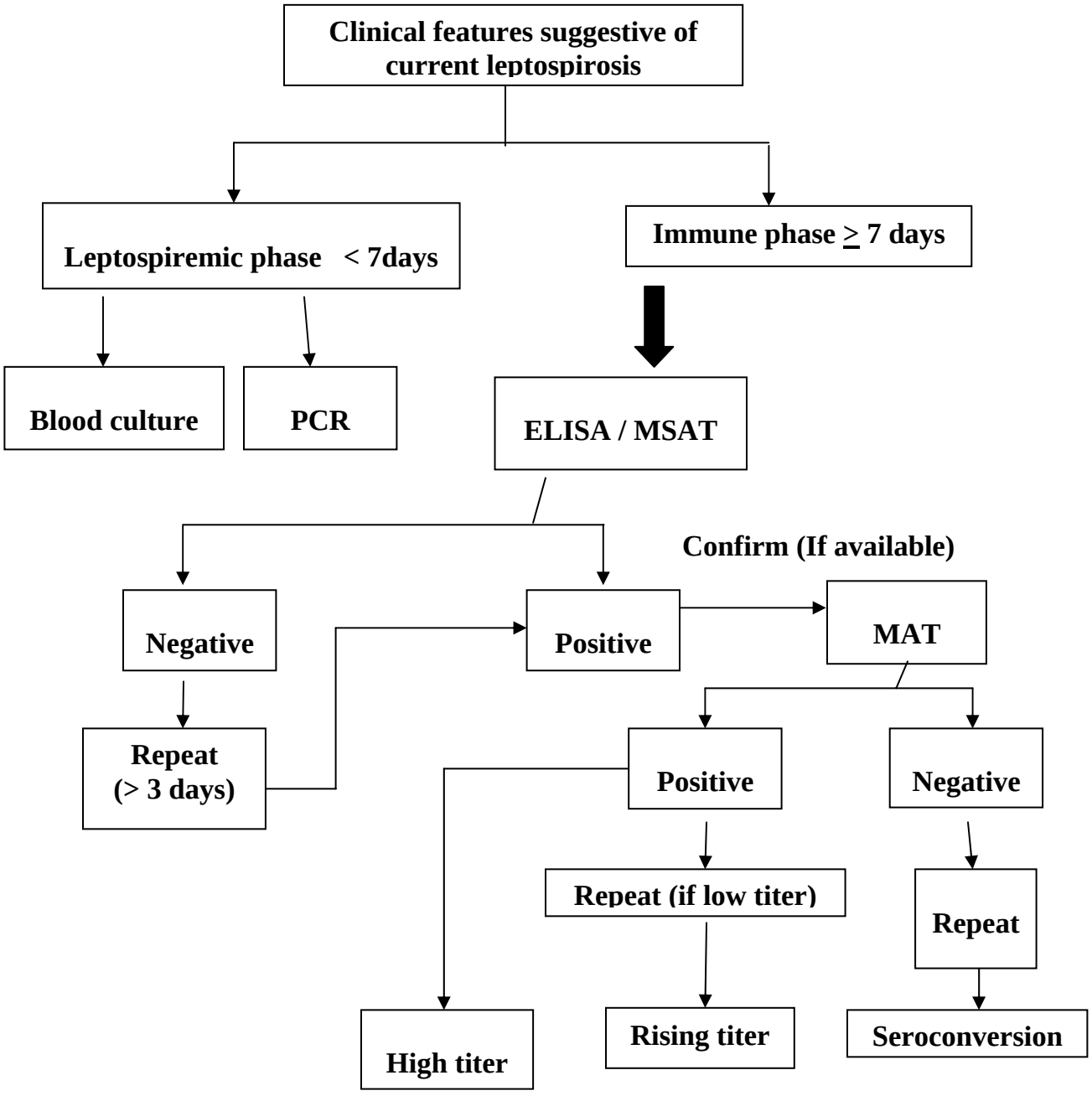
Figure:4 **Positive MSAT test**



Laboratory criteria for diagnosis of current Leptospirosis[5,11]:

1. Culture : Positive
2. MAT : a) Seroconversion / 4 fold rise in the titer
   b) High titer
3. ELISA / MSAT : Positive. An approach to the diagnosis of leptospirosis[45] is shown in table 14.

An approach to the diagnosis of leptospirosis table:14



COMMENTS

1. ELISA/MSAT are adequate for diagnosis of current infection. This can be done in smaller laboratories in both rural and urban areas. If positive,

confirm diagnosis with MAT, which would be available in larger specialized laboratories.

2. MAT – seroconversion/four fold rise in the titer is necessary for diagnosis (2^{nd} sample essential). Single high titer in MAT combined with positive ELISA/MSAT confirms the diagnosis of leptospirosis.
3. Blood culture – not sensitive.Should be done in critically ill patients. (As they may not survive to produce antibodies)[45]. The interpretation of serological tests is shown in Table 15.

Table: 15 Interpretation of serological tests

ELISA/SAT	MAT	Interpretation
+ve	Single high titer	Current infection
+ve	-ve	Current infection
-ve	Single high titer	Past infection
±ve	Sero conversion/4 fold rise in titer	Current infection

MANAGEMENT[46]:

Penicillin: is the most effective antibiotic when given early. In severe illness large doses (6 – 8 million units per day) of benzyl penicillin may be given in divided doses, preferably by IV route, for 5 – 7 days. Fever subsides in 24 to 36 hours.

Ampicillin: 1 gm IV q.i.d. in severe illness or 500 – 700 mg q.i.d. in mild illness.

Doxycycline: 200 mg/day, Amoxycillin 500 mg q.i.d

Erythromycin 250 mg q.i.d. are effective. Quinolones and Cefotaxime are also effective against leptospira.

Antibiotics are very effective only in the early stage (< 5 days). Recently there is evidence to suggest that antibiotics are useful even in the late stages of illness.

Symptomatic and Supportive Treatment:

The primary importance is the meticulous attention to fluid and electrolytes balance to prevent hypovolemia and hypotension. Fever and Myalgia can be treated with antipyretics and analgesics.

Dialysis:

Peritoneal dialysis is simple, safe and effective procedure for leptospiral acute renal failure. If the peritoneal dialysis is contraindicated hemodialysis can be done.

PROGNOSIS:

Most patients recover. Overall mortality used to be about 15 – 40% and has been reduced to about 5% with better management. Death is usually due to renal failure but it can also occur due to massive bleeding or cardiac and pulmonary complications.

GUIDELINES FOR DIAGNOSIS

Faine has evolved criteria for diagnosis of Leptospirosis on the basis of clinical, epidemiological and laboratory data (WHO guidelines)[7]. Certain necessary modifications have been made in the epidemiological (Part:B) and the laboratory criteria (Part C) of original Faine's criteria to make the diagnosis more practical in Indian institutions (Modified Faine's Criteria)[5,47]. In the Modified Faine's Criteria rapid tests (ELISA / SAT) have been introduced in Part C and Rainfall has been included in Part B to make the diagnosis early and simple. (Table:16)

The reasons for the modifications are:-

1. **Laboratory tests are essential for diagnosis:** In the original Faine's criteria, only MAT has been utilized for diagnosis. In the modified Faine's criteria, ELISA and SAT have been included with appropriate scores, as they are adequate for the diagnosis of current infection. In addition, low titers in MAT and titers based on endemicity have been eliminated. Rising titers or high titer of MAT has been retained.
2. Epidemiological factors such as rainfall and contact with contaminated environment are important for diagnosis. Most of the cases of leptospirosis are reported in the monsoon or post monsoon season.
3. Clinical features if combined with epidemiological and laboratory data confirm the diagnosis of leptospirosis.

4. Presumptive diagnosis of leptospirosis is made of:
    a. Part A or Part A & Part B score : 26 or more
    b. Part A, B, C (Total) : 25 or more
    c. A score between 20 and 25 suggests Leptospirosis as possible but unconfirmed diagnosis.

TABLE 16

Guidelines for diagnosis of leptospirosis – Original & Modified

Faine Criteria		**Modified Faine Criteria**	
Part A: Clinical data	**Score**	**Part A: Clinical data**	**Score**
Headache	2	Headache	2
Fever	2	Fever	2
Temp > 39^{O} C	2	Temp > 39^{O} C	2
Conjuntival suffusion	4	Conjuntival suffusion	4
Meningism	4	Meningism	4
Muscle pain	4	Muscle pain	4
Conjuntival suffusion Meningism Muscle pain	10	Conjuntival suffusion Meningism Muscle pain	10
Jaundice	1	Jaundice	1
Albuminuria, Nitrogen, Retention	1	Albuminuria, Nitrogen, Retention	1
Total score		Total score	
Part B: Epidemiological factors		**Part B: Epidemiological factors**	
Contact with animals or Contact with known contaminated water	10	Rainfall	5
		Contact with contaminated Environment	4
		Animal Contact	1
Total	10	Total	10
Part C : Bacteriological Lab findings		**Part C : Bacteriological Lab findings**	
Isolation of leptospira in Culture - Diagnosis certain		Isolation of leptospira in Culture – Diagnosis certain	
Positive Serology (MAT)		**Positive Serology**	
Leptospirosis –Endemic		ELISA IgM Positive	15
Single positive - Low titre	2	SAT - Positive	15
Single positive - High titre	10	MAT-Single positive in high titre	15
Leptospirosis Non endemic			
Single positive - Low titre	5		
Single positive - High titre	15	Rising titre	
Rising titre (Paired sera)	25	(paired sera)	25
Total		Total	

PATIENTS AND METHODS

PATIENTS AND METHODS

Patients admitted to the medical wards of Government Stanley Medical College Hospital with fever due to infectious disease of duration of more than 5 days who were tested positive for leptospirosis utilizing MSAT test (Macroscopic Slide Agglutination Test) (titers $\geq$ 2+) were taken up for the study.

We have utilized a simple and sensitive MSAT for early detection of leptospirosis and utilized Modified Faine's score of > 25 (Clinical (A) + Environmental (B) + Laboratory (C)) for the diagnosis of leptospirosis. All patients tested positive by MSAT were further confirmed by MAT (Microscopic Agglutination Test) with titers of $\geq$ 1:80. These patients were evaluated for relevant epidemiological, clinical and lab profiles. Patients aged >12 years were taken up for the study. The period of study was from February 2006 to May 2007.

Diagnostic Criteria:

Leptospirosis was diagnosed utilizing Modified Faine's Criteria[5] – Clinical (A), Epidemiological (B), Laboratory data (C) (Score > 25) (shown in Table 17).

Table: 17 **Diagnosis of leptospirosis-Modified Faine's Criteria**:

PART A: Clinical Data	Score	Part B: Epidemiological factors	Score
Headache	2	Rainfall	5
Fever	2	Contact with contaminated Environment	4
Temp > 39 C	2	Animal Contact	1
Conjunctival suffusion	4	Total	
Meningism	4		
Myalgia	4		
Conjunctival suffusion Meningism Myalgia	10	**Part C : Bacteriological Lab findings** Isolation of leptospira in Culture – Diagnosis certain	
Jaundice	1	**Positive Serology**	
Albuminuria / Nitrogen retension	2	ELISA IgM Positive	15
		SAT - Positive	15
		MAT-Single positive in high titre	15
		Rising titre / seroconversion	

Each feature under clinical, epidemiological and laboratory data were given appropriate scoring.

Presumptive diagnosis of leptospirosis is made of if,

Part A (or) Part (A) + (B) with a score of 26 (or) more

Part (A) + (B) + (C) = 25 or more and in serological tests, only one test should be scored.

EXCLUSION CRITERIA

Malaria, Urinary tract infection, Tuberculosis, Enteric fever, viral hepatitis and paediatric cases were excluded from the study.

The following data were noted:

1. Age, Sex, Occupation and address were noted.
2. Epidemiological profile – H/o rainfall, H/o contact with contaminated environment (Poor sanitation, poor drainage facilities, walking barefoot, recreational activities involving the contact with contaminated water and bathing in ponds), H/o animal contact (with rodents, contact with domestic animals) were noted. (shown in table 18).
3. **Table: 18 Epidemiological Profile**

Epidemiology	Cases	Percentage (%)
I. Rainfall		
II. Contact with contaminated environment i) Poor sanitation (eg.inefficient garbage disposal) ii) Walking barefoot iii) Poor Drainage facilities (eg.stagnant water) iv) Recreational activities involving the contact with contaminated water v) Bathing in ponds, lakes and wells		
III. Animal contact i) Rodents ii) Domestic animals a. Cattle b. Dogs and Cats c. Pigs		

4. Clinical features – fever, headache, myalgia, jaundice, oliguria, vomiting, loose stools, altered sensorium, dehydration, hypotension, meningeal signs and hepatosplenomegaly were noted.
5. Investigations: Hemogram, urine analysis, liver function tests, blood urea, serum creatinine, serum electrolytes, chest x-ray, ECG, Ultrasound abdomen, MSAT, MAT. (All details in proforma in annexure).

MSAT (Macroscopic Slide Agglutination Test)

This test is a valuable and simple screening test. This genus specific test is done using dense suspension of killed leptospires which is mixed with a drop of serum on a slide and rotated in a rotator (120 rpm) for four minutes. It was then examined by naked eye for presence of agglutination. A titer of 2+ and above was considered significant. The sensitivity of the test was enhanced by adding locally prevalent serovars[43].

MAT (Microscopic Agglutination Test)

This was done by standard technique and a titer of $\geq$ 1:80 was taken as significant.

MANAGEMENT

Uncomplicated leptospirosis cases were treated with oral doxycycline and severe leptospirosis (cases with organ dysfunction like renal failure, hepatic dysfunction) were treated with I.V. penicillin.

RESULTS

RESULTS

A total of 90 patients diagnosed to have leptospirosis were analyzed. There were 56 males and 34 females with mean age of 37.45 years (Table 19) In the age/sex group distribution data shows that maximum number of cases were seen in age group between 31 to 40 years (Table 20). Among the leptospirosis cases, lowest age was 13 and highest age was 74 years. As age advances, the leptospirosis incidence decreased in our study group.

Table: 19 Total number of cases

Male	Female	Total
56 (62.2%)	34 (37.7%)	90

Mean age**:** 37.45 yrs

Table: 20 Age/sex group distribution

Age	Male	Female	Total	Percentage
12 – 20	12	8	20	22.2%
21 – 30	6	8	14	15.5%
31 – 40	13	9	22	24.4%
41 – 50	9	2	11	12.2%
51 – 60	9	4	13	14.4%
61 – 70	4	2	6	6.6%
71 – 80	3	1	4	4.4%

OCCUPATION : Table 21 shows that maximum percentage of cases occurred in labourers of 71 (78.8%) cases followed by farmers (7 cases) who were outdoor manual workers.

Table :21 Occupation

Occupation	cases	Percentage
Labourers	71	78.8
Farmers	7	7.7
Housewives	7	7.7
Students	5	5.5

In our study group, the cases came predominantly from North Chennai areas surrounding our hospital. Maximum cases came from Thondiarpet (21.1%). (Table 22). (Chennai city may is enclosed in the annexure).

Table: 22 Area wise distribution of cases

Areas	Cases	Percentage
Athuthotti	1	1.1
Aathambakkam	1	1.1
Broadway	1	1.1
Chetpet	1	1.1
Dharmapuri	3	3.3
Ennore	3	3.3
Kasimedu	5	5.5
Korattur	1	1.1
Korukkupet	6	6.6
Manali	1	1.1
Nethajinagar	1	1.1
Perambur	4	4.4
Poorivakkam	1	1.1
Pulianathope	1	1.1
Redhills	8	8.8
Royapuram	6	6.6
Saidapet	1	1.1
Salem	1	1.1
Sowcarpet	5	5.5
Thondiarpet	19	21.1
Thanjavur	1	1.1
Thiruvottriyur	4	4.4
TVK Nagar	3	3.3
Uthukottai	1	1.1
Vandavasi	1	1.1
Vaniampet	1	1.1
Vannarpet	1	1.1
Viyasarpadi	8	8.8

EPIDEMIOLOGICAL FACTORS

Contact with contaminated environment occurred in 86 cases (95.5%). H/o recent rainfall within the last month of onset of fever was positive in 52 cases (57.7%). H/o animal contact was positive in 44 cases (48.8%). Out of the 86 cases who have contact with contaminated environment 86 cases came from an area from where poor sanitation existed in the form of inefficient garbage disposal. Out of 44 cases who have contact with animals 40 patients had H/o of contact with rodents and 14 cases had H/o contact with dogs and cats (shown in Table 23).

Table: 23 Epidemiological profile

Epidemiology	Cases	Percentage (%)
I. Rainfall	52	57.7
II. Contact with contaminated environment	86	95.5
i) Poor sanitation (eg.inefficient garbage disposal)	86	95.5
ii) Walking barefoot	77	85.5
iii) Poor drainage facilities (eg. stagnant water)	71	78.8
iv) Recreational activities involving the contact with contaminated water	13	14.4
v) Bathing in ponds, lakes and wells	14	15.5
III. Animal contact	44	48.8
i) Rodents	30	33.3
ii) Domestic animals		
d. Cattle	10	11.1
e. Dogs and Cats	14	15.5
f. Pigs	10	11.1

MONTHWISE DISTRIBUTION

In our study we had leptospirosis cases throughout the year with more number of cases between September to November during which time the Chennai gets monsoon rain. Intermittent rain in other months of the year and persistence of

the contaminated water would probably contributed to the cases in other months. (shown in Table 24)

Table: 24 **Monthwise distribution of cases (2006-2007)**

Month	Cases	Percentage
January	**8**	**8.8**
February	**9**	**10**
March	**4**	**4.4**
April	**5**	**5.5**
May	**4**	**4.4**
June	**3**	**3.3**
July	**5**	**5.5**
August	**6**	**6.6**
September	**11**	**12.2**
October	**24**	**26.6**
November	**8**	**8.8**
December	**3**	**3.3**

CLINICAL FEATURES

Table 25 shows the clinical features seen in our study group. All patients had fever. Headache occurred in 85 cases (94.4%), myalgia in 51 cases (56.6%), jaundice in 21 cases (23.3 %), oliguria in 15 cases (16.6 %).

Table: 25 **Clinical features-symptoms**

Symptoms	Cases	Percentage
Fever	**90**	**100**
Headache	**85**	**94.4**
Myalgia	**51**	**56.6**
Jaundice	**21**	**23.3**
Conjunctival suffusion	**6**	**6.6**
Oliguria	**15**	**16.6**
Altered sensorium	**7**	**7.7**
Fits	**1**	**1.1**
Cough with expectoration	**17**	**18.8**
Vomiting	**11**	**12.2**
Loose stools	**10**	**11.1**

Clinical features-Signs

Among the clinical signs anemia is the commonest complication found in 69 cases (76.6%), followed by jaundice in 23.3 % cases, pneumonia and splenomegaly in 6.6% cases each, hypotension and hepatomegaly in 2.2 % cases each, atrial fibrillation and quadriplegia occurred in one case each. (Table 26)

Table: 26 Signs

Signs	Cases	Percentage
Anemia	**69**	**76.6**
Jaundice	**21**	**23.3**
Hypotension	**2**	**2.2**
Pulse-Atrial fibrillation	**1**	**1.1**
Pneumonia	**6**	**6.6**
Hepatomegaly	**2**	**2.2**
Splenomegaly	**11**	**12.2**
Quadriplegia	**1**	**1.1**

HEMOGRAM

50% cases had Hb between 9 – 11 gms %, followed by 16 cases (17.7%) between 7 to 8.9 gms %, 7.7 % had Hb % between 5- 6.9 gms % . One patient had severe anemia (Hb% < 5 gms %). 21 cases (23.3%) had hemoglobin more than 11 gms %.

TOTAL COUNT AND PLATELETS COUNT

87 cases (96.6%) had total WBC count between 4000 – 11000 and 16 cases (17.7%) had platelets between 1 – 1.5 lakhs. 7 cases (7.7%) had thrombocytopenia (< l Lakh). (Table 27)

Table :27 Total count and platelets count

Total counts (cumm)	cases	percentage
< 4000	1	1.1
4000 – 11000	87	96.6
> 11000	2	2.2
Platelets		
< 1 Lakh	7	7.7
1 – 1.5 lakhs	16	17.7
> 1.5 lakhs	67	74.4

RENAL FUNCTION TESTS

16.6 % cases had renal failure with serum creatinine >1.5 mg%. 10 patients (11.1%) had serum creatinine between 1.5 – 2.9 mg%, 3 patients (3.3%) had 3 – 5 mg% and 2 patients (2.2%) had S.Creatinine > 5 mg%. 15.5 cases had Urea between 41 to 100 mg, followed by 3.3% cases had urea value between 101 – 150 mg. (shown in table 28)

Table: 28 Renal function tests

Urea (mg %)	cases	percentage
10 – 40	72	80
41 – 100	14	15.5
101 – 150	3	3.3
> 150	1	1.1
Sr.Creatinine (mg%)		
1.5 – 2.9	10	11.1
3 – 5	3	3.3
> 5	2	2.2

LIVER FUNCTION TESTS

23.3 % cases had jaundice with serum bilirubin > 1.5 mg%. Table 29 shows serum total bilirubin between 1.5 – 2.9 mg% in 9 cases (10%), in 5 cases (5.5%) between 3 – 5 mg% and 7 patients (7.7%) had bilirubin of > 5 mg%. SGOT value of between 41 – 80 IU/L occurred in 18 cases (20%) and 20% cases had > 80 IU/L. SGPT value of between 41 – 80 occurred in 22.2% cases and 15.5% cases had > 80 IU/L.

Table: 29 **Liver function tests**

Total bilirubin (mg%)	cases	percentage
1.5 – 2.9	9	10
3 – 5	5	5.5
> 5	7	7.7
SGOT (IU /L)		
0 – 40	54	60
41 – 80	18	20
> 80	18	20
SGPT (SGPT)		
0 – 40	56	62.2
41 – 80	20	22.2
> 80	14	15.5

HYPOKALEMIA

Out of 90 patients with Leptospirosis, 39 (43.3 %) patients had serum K^+ value of < 3.5 meq /L, 34.4% cases had Sr.K^+ value of between 3 – 3.5 meq/L. 5 patients had Sr.K^+ between 2.5 to 2.9 meq/L and 3 patients had Sr.K^+ < 2.5 meq/L. (shown in Table 30)

Table: 30 Hypokalemia

Sr.K^+ (meq/L)	cases	percentage
3 – 3.5	31	34.4
2.5 – 2.9	5	5.5
< 2.5	3	3.3

ECG CHANGES

16.6% cases had ST segment depression. 3 patients (3.3%) had 'U' waves of which one patient presented with quadriplegia. 3 patients (3.3%) had T wave inversion. Atrial fibrillation and atrial premature beats occurred in 1.1% cases each. In our study group, patients with normal K^+ had no ECG changes(shown in Table 31).

Table: 31 ECG changes

ECG	cases	percentage
ST depression	15	16.6
U waves	3	3.3
T wave inversion	3	3.3
Atrial premature beats	1	1.1
Atrial fibrillation	1	1.1

HYPOKALEMIA AND ECG CORRELATION

34.4% cases had Sr.K^+ between 3 – 3.5 meq/L of which 16.6% cases had ST segment depression. 5 patients had Sr.K^+ between 2.5 – 3 meq/L of which 3 patients had 'T' wave inversion and one had atrial premature beats and another had 'U' wave. 3.3 % cases had S.K+ < 2.5 meq /L of which 2 cases had U waves and one had atrial fibrillation (shown in Table 32).

Table :32 Hypokalemia and ECG correlation

Sr.K^+			E C G		
Level (meq/L)	Cases	%	Changes	cases	%
3 – 3.5	31	34.4	ST depression	15	16.6
2.5 – 2.9	5	5.5	'T' inversions	3	3.3
			Atrial premature beat	1	1.1
			'U' Wave	1	1.1
< 2.5	3	3.3	'U' Wave	2	2.2
			Atrial fibrillation	1	1.1

USG ABDOMEN

Splenomegaly was seen in 12.2% cases, hepatomegaly in 2.2 % cases followed by hepatosplenomegaly in 3.3% cases (Table 33).

Table: 33 USG abdomen

USG Abdomen	cases	percentage
Hepatomegaly	2	2.2
Hepatosplenomegaly	3	3.3
Splenomegaly	11	12.2

MSAT SCORING

Table 34 shows MSAT scoring of 2+ in 84.4% cases and 3+ score in 15.5% cases.

Table: 34 MSAT Scoring

MSAT	Cases	percentage
2+	76	84.4
3+	14	15.5

MODIFIED FAINE'S SCORING

Table 35 shows that 43.3% cases had Modified Faine's Score between 25 – 30 and 28.8 % cases had score of between 31 – 35.

Table: 35 Modified Faine's Scoring

Score	cases	percentage
< 25	5	5.5
25 – 30	39	43.3
31 – 35	26	28.8
36 – 40	18	20
> 40	2	2.2

By Microscopic Agglutination Test (MAT), Ictero was the commonest serovar identified in 33.3 % cases in our study. Chest X ray revealed pneumonia in 6.6% cases and in 13.3% cases Peripheral smear was consistent with microcytic hypochromic anemia.

ARDS (Acute Respiratory Distress Syndrome) occurred in one patient in whom arterial blood gas analysis revealed metabolic acidosis with respiratory alkalosis. Quadriplegia and atrial fibrillation occurred in one patient each.

All patients who were severely ill (organ dysfunction) were treated with I.V. Penicillin.Third generation cephalosporins (cefotaxime) were used in those who were allergic to penicillins. All mild cases were treated with oral doxycycline. Table 36 shows the drugs used in our study group. Patients with hypokalemia were treated with oral potassium and severe hypokalemia (S.K+ < 2.5 meq /L) was treated with parenteral potassium therapy.

Table: 36 Treatment

Drugs	cases	percentage
Doxycycline	70	77.7
Penicillin	16	17.7
Cefotaxime	4	4.4

There were no mortality. One patient underwent hemodialysis.

DISCUSSION

DISCUSSION

Leptospirosis has been under diagnosed and under reported from India due to a lack of awareness of the disease and lack of appropriate laboratory diagnostic facilities in most parts of the country[1,2]. Leptospirosis has long been considered a rare zoonotic disease in India with only sporadic cases being recorded. Since 1980's the disease has been reported from various states during monsoon months in mini epidemic proportions. The disease is endemic in Kerala Tamilnadu, Gujarat, Andamans, Karnataka, Maharashtra.It has also been reported from Andhra Pradesh, Orissa, West Bengal, Uttar Pradesh, Delhi & Puducherry[3,4].

The problem of under diagnosis is because of complicated diagnostic tests. In the first week of illness blood culture or PCR is diagnostic but the culture reports may take weeks or months to become positive. PCR is promising on both sensitivity and specificity, but is complicated and expensive. Hence, the serological tests are used for diagnosis, since the clinical features of leptospirosis are non-specific[46].

MAT (Microscopic Agglutination Test) is the gold standard test for diagnosis of leptospirosis. But it is complicated, not useful for early diagnosis, less sensitive requires two samples for diagnosis.

Simple genus specific tests such as SAT and ELISA have become available which have made the diagnosis easy. ELISA detects specific IgM antibodies thus helping in rapid diagnosis of current infection. But it is expensive. MSAT

(Macroscopic Slide Agglutination Test) is a simple, rapid and sensitive diagnostic test for current leptospirosis becoming positive as early as 5th day of illness. It can be done in small laboratories also[5,44,47].

A simple scoring criteria (Modified Faine's Criteria)[5,47] is recommended for diagnosis of leptospirosis in Indian set up. This has been modified from the original Faine's criteria (WHO Guidelines)[7] to make the diagnosis simple and to detect the illness early. In this study Modified Faine's criteria was utilized for diagnosis of Leptospirosis along with MSAT (All samples were confirmed by MAT).

A total of 90 cases were taken up for the study. In these patients 56 (62.2%) cases were males and 34(37.7%) cases were females. The mean age was 37.45 years. This study was undertaken in our hospital, Government Stanley Medical College Hospital that caters mainly to the population of North Chennai. Majority of cases in our study came from North Chennai. Majority of lower socio economic status population live in the North Chennai. Contaminated environment, poor sanitation facilities and stagnant contaminated water are prevalent here. Majority of North Chennai people are out door manual workers. 6 cases (6.6%) in our study group came from outside Chennai. (shown in Table 22).

In our study the lowest age group was 13 years and the highest age group was 74 years. The maximum affected age group was between 31 – 40 years constituting 24.4% of cases. In these 13 cases were males and 9 cases were females. The next most common age group affected was between 12 – 20 years

(22.2%) and 21 – 30 years age group (15.5%). The least affected age group was > 70 years (4.4%) of age group (shown in table 20) . This explains the fact that the middle and young group were commonly affected with leptospirosis than the age group > 60 years. The age group between 20 to 50 years is the economically productive period and during which period they have high chance of occurring contact with contaminated environment. This may be related to the "way of life" as well as to specific occupations[10].

This was consistent with a study from Barbados[15] in which 235 patients were studied. Males (173 cases) predominated in the group. 62 cases were females and 93 patients of both sexes aged between 15 – 34 years were maximum affected 39.5% cases. In this study men are more commonly affected than females and this was also consistent with our study.

Contaminated environment is due to poor environmental hygiene, which is contributed by the following factors.

1. Rainfall
2. Poor sanitation (inadequate garbage disposal which can attract rodents)
3. Poor drainage facilities (e.g. stagnant water)
4. The above factors can attract cattle, pigs, rodents and stray dogs which are potential source for infection.
5. With all the above factors walking barefoot, recreational activities involving the contact with contaminated water and bathing in ponds, lakes and wells

poses a potential risk, when coming in contact with stagnant water or infected soil.

Contact with contaminated environment is most important epidemiological risk factor. In our study contact with contaminated environment occurred in 86 cases (95.5%).

History of recent rainfall within the previous one month of the onset of fever was positive in 52 cases (57.7%). Poor sanitation facilities (eg.inefficient garbage disposal) was the (95.5%) most important epidemiological risk factor found in our study group. This is followed by history of walking barefoot in 77 cases (85.5%) in the contaminated environment. In 71 cases (78.8%), exposure to poor drainage facilities. (eg. stagnant water) was present. In 14.4% cases history of recreational activities involving the contact with contaminated water was present. In 15.5% cases had history of bathing in contaminated water sources like in ponds/lakes/wells present (Table.23)

In 48.8% cases of animal contact was present. In 33.3% cases history of contact with rodents was present of which one patient had the job involving the removal dead rats and the other had the hobby of putting eatables to the rats whose house was heavily infested with rats. Among the patients who had contact with animals, significant number had contact with domestic animals. In our study group all the farmers and some of the labourers had exposure to domestic animals such as cattle, dogs, cats and pigs. The data on exposure to domestic animals was

shown in Table.23. This study highlights the importance of contact with contaminated environment being the most important risk factor.

In our study we had leptospirosis cases throughout the year with more number of cases between September to November during which time the Chennai gets monsoon rain. In other months, the persistence of contaminated environment was responsible for the transmission of leptospires to man. This contrasts with the study done during 1987 – 93[11] where 90% cases reported during monsoon months. The monthly incidence comparison of cases with our study is shown in Table.37

Table: 37 Monthly incidence comparision of leptospirosis cases

Month	Leptospirosis in Chennai 1987 – 93[11] n=176 (%)	Our study n=90 (%)
January	2.8	8.8
February	0.5	10
March	--	4.4
April	--	5.5
May	--	4.4
June	--	3.3
July	0.5	5.5
August	--	6.6
September	2.2	12.2
October	--	26.6
November	56	8.8
December	36.4	3.3

Occupation plays an important role in the risk of acquiring infection. Leptospirosis is common in high risk groups which include agricultural workers, outdoor manual workers, abattoirs, miners, veterinarians and also any one

venturing outside in an environment which has water, infected soil and infected animals.

In our study group, 71 cases (78.8%)were labourers and 7 cases (7.7%) were farmers. Thus the outdoor manual workers predominated in our group. These patients had direct contact with the contaminated environment (Table 21). 7 cases were housewives and 5 cases were students who had contact with the contaminated environment while playing in the schools. Among the 71 cases of labourers one patient had the job of removing of dead rats and the other patient had the hobby of putting eatables to the rats whose house was heavily infested with rats. The inter-relationship between the occupations, contaminated environment and home and leisure activities is shown in table 5. This was consistent with the previous Chennai study in which the outdoor manual work was associated with 49% of cases and 61.3% cases were associated with outdoor work[8] (Table 2).

Outdoor manual workers are more vulnerable while they come in contact with contaminated environment. Leptospirosis is a zoonosis and infected animals (rodents and domestic animals) are an important source of infection. Contaminated environment is due to the urine of these infected animals contaminating the soil and water and contact with this leads to human infection.

Everard & Everard pointed out that where leptospirosis is widespread in the environment and where the disease is endemic, infection will be related to a way

of life as well as to specific occupations. Thus when there are large number of rodents, stray dogs and wild animals, where people drink or bathe in untreated water, when sewerage and drainage facilities are inadequate and where open shoes or none at all worn, leptospiral infection can be common. In such places occupational risk factors are so vertically linked with life style risk factors then investigation of sources of infection in individuals are inappropriate. That in Chennai, the general truth applies that maleness, heavy rainfall and outdoor manual occupations encourage higher incidence rate of leptospirosis and that more specific sources cannot be pinpointed with certainty[8].

In the 90 patients of our study group, fever (100%), headache (94.4%), myalgia (56.6%) were the common clinical features noted. In the South Vietnam study fever (97%), headahce (98%), myalgia (79%) were noted. In Hawaii study[14], fever (99%), headache (89%) and myalgia (91%) were noted. Anicteric presentation in our study was 76.6%, which is more than the Hawaii study, but less than the South Vietnam study. 23.3 % cases had jaundice in our study group which is higher than the South Vietnam study[48]. 16.6 % cases had renal failure in our study which is lower than Hawaii study but it is higher than the South Vietnam study. Conjunctival suffusion (6.6%), altered sensorium (7.7%), Vomiting (12.2%), loose stools (11.1%) were the other features in our study group. The comparison between the clinical features of our study, South Vietnam study and Hawaii study is shown in Table 38.

Table: 38

Clinical features	South Vietnam[48] n=150 (%)	Hawaii Study[14] n=353 (%)	Our Study n = 90 (%)
Fever	97	99	100
Headache	98	89	94.4
Myalgia	79	91	56.6
Conjunctival suffusion	42	28	6.6
Meningism	12	27	7.7
Vomiting	33	73	12.2
Diarrhoea	29	53	11.1
Anicteric presentation	98	61	76.6
Hypotension	--	--	2.2
Cough	20	--	18.8
Hepatomegaly	15	16	4.4
Splenomegaly	22	9	6.6
Jaundice	2	39	23.3
Renal failure	4.6	26	16.6

While comparing our study with the Indian studies, fever (100%) was consistent as like in Mumbai and Gujarat studies[1]. Jaundice (23.3%) was low in our study group than comparing the Mumbai[41] (33.7%) and Kerala studies[13] (80%), The oliguria was high in Mumbai (28.3%), Kerala (59%) and Gujarat (46%) studies than our study (16.6%) (Table. 39).

Table: 39 Indian studies : clinical features comparision

Clinical features	Mumbai[41] n=74 (%)	Kerala (Kottayam)[13] n=900 (%)	Gujarat (Surat)[1] n=80 (%)	Our Study n=90 (%)
Fever	100	95	100	100
Headache	91.8	53	--	94.4
Myalgia	67.5	85	--	56.6
Conjunctival suffusion	35.1	65	58	6.6
Cough	35.1	--	13	18.8
Jaundice	33.7	80	--	23.3
Oliguria	28.3	59	46	16.6

In our study group 50% cases had Hb% between 9 – 11 gms%, followed by 16 cases (17.7%) had Hb% between 7 to 8.9 gms%. One patient had severe anemia (Hb < 5gms%). 21 cases (23.3%) had hemoglobin more than11 gms%. Occult blood loss from G.I tract due to leptospirosis and already existing anemia may be the reasons for anemia.

87 cases (96.6%) had total WBC count between 4000 – 11000 and 16 cases (17.7%) had platelets between 1– 1.5 lakhs. 7 cases (7.7%) had thrombocytopenia (< 1 lakh) (Table. 27).

Jaundice is an important complication indicating the severity of illness, which occurs between 4^{th} to 6^{th} day of illness. Marked elevation of bilirubin with mild elevation of transaminases is characteristic. Serum total bilirubin > 1.5 mg% is taken as indicative of liver injury in our study group. Jaundice occurred in 23.3% cases (Table 30). 5.5 %cases had S.bilirubin between 3 – 5 mg%, 7.7% cases had S.bilirubin > 5 mg% and 10 % had S.bilirubin between 1.5 – 2.9 mg %. In 20% cases SGOT ranged between 41 – 80 IU /L. In 22.2% cases SGPT ranged between 41 – 80 IU /L. SGOT and SGPT were < 40 IU /L in 60% and 62.2% cases respectively. In Barbados study jaundice was 95% and in the previous Chennai study it was 84% (1990) (Table 40). The probable explanation for this shift could be due to improved diagnostic facilities in diagnosing leptospirosis and investigating all fever patients for leptospirosis with fever > 5 days of duration. Anicteric presentation in our study was 76.6%.

Table: 40

Clinical features	Barbados study[39] n=88 (%)	United States study[12] n=345 (%)	Korea study[40] n=93 (%)	Chennai study[8] n=57 (%)	Our study n=90 (%)
Fever	**85**	**100**	**97**	**100**	**100**
Myalgia	**49**	**68**	**88**	**72**	**56.6**
Conjunctival suffusion	**54**	**68**	**88**	**58**	**6.6**
CNS complications	**2**	**21**	**6**	**12**	**7.7**
Jaundice	**95**	**43**	**16**	**84**	**23.3**
Renal failure	**49**	**26**	**15**	**72**	**16.6**
Anicteric presentation	**5**	**57**	**84**	**16**	**76.6**

Renal failure is another important life threatening complication of leptospirosis. It is the commonest cause of death in leptospirosis. In our study 16.6% cases had renal failure (Table 29). We have taken Sr. creatinine of > 1.5 mg% to indicate renal failure and to diagnose the organ dysfunction early and to start them on aggressive parenteral therapy. Mild renal failure (Sr. Cr: 1.5 – 2.9 mg%) occurred in (11.1%) cases, moderate renal failure (S.Cr: 3 – 5 mg %) in 3.3% cases and severe renal failure in 2.2 % cases (S.Cr. > 5 mg%). In comparing the Barbados study[39] (49%), United States study[12] (26%) and previous Chennai Study[8] (72%), our study group had less number of renal failure patients probably due to investigating all patients with fever > 5 days duration for leptospirosis (table 40).

Hypokalemia is an important electrolyte disturbance in leptospirosis due to excessive renal loss of K+ due to blockage of Na + K+ ATPase in the ascending limb of loop of Henle. Hypokalemia in leptospirosis marks the severe illness[33,34]. Out of 90 patients with leptospirosis, 39 patients (43.3 %) had serum K^+ value of < 3.5 meq /L. 34.4% cases had Sr.K^+ value of between 3 – 3.5 meq/L. 5.5 % patients had Sr.K^+ between 2.5 to 2.9 meq/L and 3 patients had Sr.K^+ < 2.5 meq/L. (shown in table 30)

Sudden death can occur in leptospirosis due to myocarditis and atrial fibrillation is the common arrhythmia observed in leptospirosis. ECG changes in leptospirosis denotes the severity of illness[27-32]. It may be due to hypokalemia but however ECG changes due to myocarditis cannot be ruled out. In our study 16.6% cases had ST segment depression. 3 patients (3.3%) had 'U' waves of which one patient presented with Quadriplegia. 3 patients (3.3%) had T wave inversion. Atrial fibrillation and atrial premature beats occurred in 1.1% cases each. In our study group, patients with normal K^+ had no ECG changes (shown in table 31).

In our study, 34.4% cases had Sr.K^+ between 3 – 3.5 meq/L of which 16.6% cases had ST segment depression. 5 patients had Sr.K^+ between 2.5 – 3 meq/L of which 3 patients had 'T' wave inversion and one had atrial premature beats and another had 'U' wave (shown in table 32).

Ultrasound abdomen revealed splenomegaly in 12.2% cases followed by hepatosplenomegaly in 3.3% cases and hepatomegaly in 2.2 % cases (Table 33). Chest X ray revealed pneumonia in 6.6% cases. Reports of leptospirosis producing

pneumonia came from Andaman and Nicobar Islands. It is endemic for leptospirosis since early part of the 20th century. Out breaks of Andaman Haemorrhagic fever (AHF) were reported since 1988. This was proved to be leptospirosis in 1994. 524 cases of AHF (leptospirosis) were reported from 1988- 97[3,22,23]. The disease presented as febrile illness with pulmonary haemorrhage during post monsoon periods. As the disease presented with predominant pulmonary involvement, a leptospiral etiology was never considered. In addition, absence of diagnostic facilities was responsible for not diagnosing leptospirosis[22].

In our study, MSAT scoring of 2+ occurred in 84.4% cases and 3+ score in 15.5% cases.(Table: 34). Ictero is the commonest serogroup identified by MAT in 33.3 % cases. 43.3% cases had Modified Faine's Score between 25 – 30 and 28.8 % cases had score of between 31 – 35 (Table :35). Other features noted in our study were altered sensorium in 7.7 % cases, fits in one patient , cough with expectoration in 18.8 % cases, vomiting in 12.2 % cases and loose stools in 11.1 % cases (Table:25).

ARDS (Acute Respiratory Distress Syndrome) occurred in one patient in whom arterial blood gas analysis revealed metabolic acidosis with respiratory alkalosis. Quadriplegia and atrial fibrillation occurred in one patient each.

All patients who were severely ill (organ dysfunction) were treated with I.V. Penicillin.Third generation cephalosporins (cefotaxime) were used in those who were allergic to penicillins. All mild cases were treated with oral doxycycline. Table 36 shows the drugs used in our study group. Patients with hypokalemia were

treated with oral potassium and severe hypokalemia (S.K+ < 2.5 meq /L) was treated with parenteral potassium therapy. Adequate hydration and antipyretics and other supportive measures were also given There were no mortality. One patient underwent hemodialysis.

In our study complicated leptospirosis is significantly less compared to previous studies from Chennai. This study highlights that anicteric leptospirosis was the common presentation in Chennai due to screening of all fever patients utilizing Modified Faine's criteria.

We conclude that contact with contaminated environment [poor sanitation (e.g. inefficient garbage disposal), poor drainage facilities (e.g. stagnant water)] walking in barefoot, recreational activities involving the contact with contaminated water and bathing in contaminated water sources like in ponds, lakes and wells and animal contact along with recent rainfall are important epidemiological risk factors in acquiring leptospirosis. High risk occupational groups involving the contact with the above factors are vulnerable. Hypokalemia and ECG changes are important markers of severe leptospirosis as like renal and hepatic dysfunctions.

Early identification of Leptospirosis utilizing Modified Faine's criteria will prevent serious complications. Early identification of organ dysfunctions and energetic treatment will decrease the mortatlity due to leptospirosis. Preventive measures like antirodent measures, isolation of index case domestic animals and control of transmission along with public health measures to improve the

contaminated environment will run a long way to decrease not only leptospirosis but also other communicable diseases. Thus, we recommend that all patients with fever of more than 5 days of duration should be investigated for leptospirosis utilizing simple screening test such as MSAT especially in endemic areas.

SUMMARY

SUMMARY

1. 90 patients with leptospirosis were analyzed. (males – 56, females – 34 and mean age was 37.5 years).
2. Contact with the contaminated environment is the important risk factor in acquiring leptospirosis. The contact with contaminated environment occurred in 95.5% cases followed by rainfall 48.8% and animal contact in 48.8% cases. Most cases occurred in monsoon months but have also occurred in non-monsoon months due to the intermittent rainfall and persistence of the contaminated environment.
3. Poor sanitation (inefficient garbage disposal) is the most important epidemiological risk factor and it occurred in 95.5% cases along with walking in barefoot in 85.5% cases. Poor drainage facilities (stagnant water) occurred in 78.8% cases, recreational activities involving the contact with contaminated water occurred in 14.4% cases and bathing in contaminated water sources like in ponds, lakes and wells occurred in 15.5% cases.
4. Among the animal contact, the contact with rodents occurred in 33.3% cases. Among the domestic animals, the contact with cattles occurred in 11.1% cases, and the contact with dogs/cats and pigs occurred in 15.5% and 11.1% cases respectively.

5. Anicteric Leptospirosis (76.6%) was the commonest clinical presentation of leptospirosis noted in our study group. Fever, headache, myalgia were the common clinical presentations. Conjunctival suffusion and meningism were rare.
6. Jaundice occurred in 23.3% cases. Renal failure occurred in16.6% cases. (mild renal failure – 11.1%; Moderate renal failure 3.3%; Severe renal failure – 2.2%). One patient underwent hemodialysis.
7. 43.3% cases had hypokalemia ($Sr.K^+ < 3.5$ meq/L);
    a. Sr.K+ : 3 – 3.5 meq/L occurred in 31.4% cases
    b. Sr.K+ : 2.5 – 2.9 meq/L occurred in 5.5% cases
    c. Sr.K+ < 2.5 meq/L occurred in 3.3% cases

   ST segment depression was the commonest ECG manifestation noted in the mild hypokalemia cases($Sr.K^+$ - 3 to 3.5 meq/L). One patient had quadriplegia and another patient had atrial fibrillation in whom $Sr.K^+$ was < 2.5 meq/L.
8. Thrombocytopenia occurred in7.7% cases. 6.6% cases had pneumonia. One patient had adult respiratory distress syndrome (ARDS).
9. Modified Faine's criteria scoring of 25 – 30 occurred in 43.3% cases, 31 – 35 in 28.8% cases and 36 – 40 in 20% cases. Modified Faine's Criteria was valuable in the diagnosis of leptospirosis especially the anicteric leptospirosis.
10. All patients recovered and no mortality.

CONCLUSION

CONCLUSION

1. This study has revealed the role of contaminated environment in the transmission of leptospirosis. Among the contact with contaminated environment, poor sanitation (inefficient garbage disposal) and walking barefoot are the most important epidemiological risk factors. Recreational activities and bathing in the contaminated water, rainfall and animal contact are the other epidemiological risk factors. Leptospirosis can also occur in non-monsoon months due to the persistence of the contaminated environment. Out door manual workers are at risk of acquiring leptospirosis.
2. Anicteric Leptospirosis (76.6%) is the commonest clinical presentation. Lower incidence of jaundice and renal failure are noted.
3. Hypokalemia and ECG changes in leptospirosis are also the important markers of severe illness as like renal and hepatic dysfunctions.
4. There were no mortality.
5. Modified Faine's Criteria with simple diagnostic test such as MSAT makes the diagnosis easy, simple and early and decreases the mortality due to leptospirosis. It is recommended that all fever patients should be evaluated for leptospirosis especially in endemic areas.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Singh J & Sokhey J. Epidemiology, Presentation & Control of leptospirosis. *Proceedings of the third round table conference. Series-leptospirosis. Ranbaxy science foundation*(3);1998: 17-31
2. Rao RS, Gupta N, Bhalla P et al. Leptospirosis in India and the rest of the world. *Braz J infec Dis* 2003; 7(3) 178-193.
3. Report of the Brainstorming meeting on Leptospirosis Prevention and control.Mumbai, 16- 17 February 2006. Joint Publication by Office of WHO, Representative to India, New Delhi and Regional Medical Research Centre (ICMR), WHO Collaborating Centre for Diagnosis, Research, Reference and Training in Leptospirosis.
4. Kamath SA, Joshi SR. Re-emerging infections in urban India – Focus Leptospirosis. .*J.Assoc Phys India* 2003,51:247-248
5. Shivakumar S, Shareek PS. Diagnosis of Leptospirosis – Utilizing modified faine's criteria. *J.Assoc.Phys India* 2004, 52 : 678 – 679
6. Feigin RD, Anderson DC. Human Leptospirosis. *CRC Cri Rev lab sci*. 1975; 5: 413-67
7. Faine S. guidelines for the control of Leptospirosis. *WHO offset publication*. 1982;21- 67, Geneva
8. Muthusethupathi MA, Shivakumar S, *et al.* Leptospirosis in Chennai – A clinical and serological study. *J. Assoc phys India* 1995;43:456-58.
9. Everard JD, Everard CM; Leptospirosis in the Caribbean. *Reviews in Medical Microbiology*, 1993; 4: 114-221
10. Muthusethupati MA, Shivakumar S et al. A Hand book of Human Leptospirosis. *South Asian Work shop on Diagnostic Methods in Leptospirosis (SAWDIL).* Madras.1995: 2-31.

11. Muthusethupathi MA, Shivakumar S, *et al.* Leptospirosis in Madras,1987–93, *South Asian Workshop on Diagnostic methods in Leptospirosis.* 1995:61.
12. Heath CW, Jr.Alexander AD, and Galton MM. Leptospirosis in the United States. *N Engl J Med* 1965; 273.
13. Vimala, Kasi Visweswarn, Leptospirosis in Kottayam (Kerala), *South Asian Workshop on Diagnostic methods in Leptospirosis*. 1995:61.
14. Katz et al. Assessment of the clinical presentation and treatment of 353 cases of laboratory confirmed Leptospirosis in Hawaii, 1974-1998. *Clinical Infectious Diseases* 2001;33:1834-41.
15. C.O.R.Everard, S.Bennett et al. An investigation of some risk factors for severe Leptospirosis on Barbados. *Journal of Tropical medicine & hygiene.* 1992;95: 13 – 22.
16. C.O.R.Everard, A Serosurvey for Leptospirosis in Trinidad among urban and rural dwellers and persons occupationally at risk. *Trans.Roy.Soc.Trop.Med.Hyg. 1985; 79: 96 – 105*
17. Clerke AM,Leuva AC, Joshi C et al. Clinical profile of leptospirosis in south Gujarat. *J Post Grad Med 2002. 48: 117-118.*
18. Patel BK, Gandhi SJ, Desai DC. Clinico-epidemiological aspects of leptospirosis in south Gujarat. .*Indian J Med Microbiol 2006 24(4). 322-326.*
19. Karande S, Kulkarni H, Kulkarni M et al. Leptospirosis in children in Mumbai slums. (2002). *Indian Journal of Pediatrics* 69, 855-858.
20. Karande S, Bhatt M, Kelkar A et al. An observational study to detect leptospirosis in Mumbai , India 2000. *Archieves of disease in childhood*.2003. 88(12) 1070-1075.
21. Terepstra et al. Human Leptospirosis: *Guidelines for Diagnosis, Surveillance & Control (WHO)* 2003:1 – 109
22. SehgalSC, Emergence of leptospirosis as a public health problem. *Proceedings of the third round table conference.Series-leptospirosis.Ranbaxy science foundation*(3);1998: 7-12.

23. Singh SS, Vijayachari P,Sinha A et al. Clinical- Epidemiological study of hospitalized cases of severe leptospirosis. *Indian J Med Research* 1999.109:94-9

24. Muthusethupati MA, Shivakumar S, Vijaykumar R et al. Renal involvement in Leptospirosis- Our Experience in Madras City. *J Post Grad Med1994;40(3):127-31.*

25.Jayakumar M, Ram Prabakar H, Edwin Fernando M et al. Epidemiologic trend changes in acute renal failure – A tertiary centre experience from South India. *Renal Failure* 2006; 28:405-10.

26.Shivakumar S. Leptospirosis in Chennai- Changing clinical Profile. *J.Assoc Phys India* 2006,54:964-965.

27.H.S.Moore. ECG changes in leptospirosis. Br. Med. J.September 4, 1965. 2(5461): 594.

28.D' Sonza CC, Dwivedi SS, Balasubramanian RR. Leptospirosis with Atrial flutter (a case report). *J Post Grad Med 1990. (36) 222- 4.*

29. Dixon A.C. The cardiovascular manifestations of leptospirosis. *West J Med. 1991 March; 154(3): 331–334.*

30. A. Pertzelan AND W. Pruzanski *Leptospira Canicola* Infection: Report of 81 Cases and Review of the Literature *.Am. J. Trop. Med. Hyg., 12(1), 1963. 75-81*

31.Paul N. Levett. Leptospirosis. Clin Microbiol Rev. 2001 April; 14(2): 296–326

32.Watt G, Padre LP et al. Skeletal and cardiac muscle involvement in severe, late leptospirosis. *J Infct Dis. 1990 Jul;162(1):266-9.*

33.Visith S, Kearkiat P. Nephropathy in leptospirosis. *J. Post. Grad. Med* 2005. (51); 184-188

34.Krishnan A, Dilip R. Paralysis due to renal potassium wasting: an unusual presentation of leptospirosis. Nephrol Dial Transplant (2003) 18: 2454-2455

35.Shivakumar S, Emmanuel Baskar et al. *J. Assoc.Phys. India (abstract)* 2003; 51:1257.

36. Jayakumar M, Ram Prabakar H, Edwin Fernando M et al. Epidemiologic trend changes in acute renal failure – A tertiary centre experience from South India. *Renal Failure* 2006; 28:405-10.

37. Muthusethupathi M.A., Shivakumar S, et al. Acute Renal Failure in Madras City – Changing Profile. *IJN (new series),* 1995;3:66 – 70.

38. Muthusethupati MA, Shivakumar S. Leptospirosis in Madras,India- A study of 206 cases(1987-95). First meeting of the International Leptospirosis Society, Nantes(France).September 1996.9-13.

39. Edwards. C.N. Nicholson GD, Hasell TA et al. Leptospirosis in Barbados – A clinical study, *WI. Med. Jn.* 1990;39 : 27 – 34

40. Park YK, Park YK, Rhee YK, Kang SK. Leptospirosis in the Chenbuk province of Korea in 1987, *Korean J. Int. Med.* 1990;5 : 34 – 43

41. Renu Bharadwaj, Abhijit M. Bal et al, An Urban outbreak of Leptospirosis in Mumbai, India. 200. *Jpn. Jn. Inf.Dis.* 2002;55 : 194 – 96

42. Angelo P Brendo *et al.* Macroscopic agglutination test for rapid diagnosis of Heman Leptospirosis. *Journal of Clinical Microbiology (*1998);36(11):3138 – 3142.

43. Sumathi G, Chinari Pradeep KS and Shiva Kumar S. MSAT – A screening test for Leptospirosis. *Indian J Med Microbiol* (1997) – 15 : 84.

44. Chinari Pradeep KS, Sumathi G, Vimala RangaRao G, Shivakumar S Leptospirosis laboratory. Chennai Medical College – A three year experience in sero- diagnosis (1995-1997). *Indian J Med Microbiol* (1999) 17(10): 50-51.

45. Shivakumar S, Krishnakumar B. Diagnosis of Leptospirosis – Role of MAT. *Jn.Assoc.Phys.India.* 2006; 54: 338

46. Shivakumar S. Approach to Leptospirosis in India. Bhattacharya PK (Ed);Medicine Update-APICON,Assam,2003; 699-703.

47. Shivakumar S. Leptospirosis – Evaluation of clinical criteria *J.Assoc Phys India* 2003, 51 : 329 – 330

48. Steven J Berman M.D., Che-chang Tsai et al. Sporadic Anicteric Leptospirosis in South Vietnam. *Annals of Internal Medicine.* 1973; 79: 167 – 73

ANNEXURE

PROFORMA

Name	:	Date of Admission	:
Age	:	Date of Discharge	:
Sex	:	I.P. No.	:
Address	:		
Occupation	:		

Clinical Data

Fever (duration)	:	Cough with expectoration	:
Headache	:	Abdominal pain	:
Myalgia	:	Altered sensorium	:
Jaundice	:	Oliguria, dysuria	:
Vomiting	:	Bleeding diathesis	:
Diarrhoea	:		

Examination

Anemia, jaundice, lymphadenopathy, conjunctival suffusion, muscle tenderness, volume status (severity of dehydration)

Vitals: Blood Pressure, Pulse Rate, Respiratory Rate, Temperature

Systemic Examination:

CVS : (Hemodynamic status, evidences for arrythmias)

RS : (Evidences for pneumonia)

ABD : (Hepatosplenomegaly)

CNS : (Meningeal signs)

Epidemiological Data:

1. Rainfall
2. Contact with contaminated environment. (Poor sanitation, poor drainage facilities, walking barefoot, recreational activities involving the contact with contaminated water and bathing in ponds).
3. H/o animal contact

Epidemiology	Cases	Percentage (%)
I. Rainfall		
II. Contact with contaminated environment **i) Poor sanitation (eg.inefficient garbage disposal)** **ii) Walking barefoot** **iii) Poor drainage facilities (eg.stagnant water)** **iv) Recreational activities involving the contact with contaminated water** **v) Bathing in ponds, lakes and wells**		
III. Animal contact **i) Rodents** **ii) <u>Domestic animals</u>** **g. Cattle** **h. Dogs and Cats** **i. Pigs**		

DIAGNOSIS OF LEPTOSPIROSIS-MODIFIED FAINE'S CRITERIA:

PART A: Clinical Data	Score	Part B: Epidemiological factors	Score
Headache	2	Rainfall	5
Fever	2	Contact with contaminated Environment	4
Temp > 39 C	2	Animal Contact	1
Conjunctival suffusion	4	Total	
Meningism	4		
Myalgia	4		
Conjunctival suffusion		**Part C : Bacteriological Lab findings**	
Meningism	10	Isolation of leptospira in Culture –	
Myalgia		Diagnosis certain	
Jaundice	1	**Positive Serology**	
Albuminuria / Nitrogen retension	2	ELISA IgM Positive	15
		SAT - Positive	15
		MAT-Single positive in high titre	15
		Rising titre / seroconversion (paired sera)	25

diagnosis of leptospirosis is made of if,

Part A (or) Part (A) + (B) with a score of 26 (or) more

Part (A) + (B) + (C) = 25 or more and in serological tests only one test should be scored.

INVESTIGATIONS

Hemogram	:	Hb, TC, DC, ESR
Platelet count	:	
Urine analysis	:	Albumin, sugar, deposits
Renal function test	:	Blood urea, serum creatinine
Serum Electrolyte	:	Na^+, K^+
Liver Function Test:		Serum bilirubin (total and direct), SGOT, SGPT, SAP, serum total protein and albumin

Chest X-ray

ECG

Ultrasound abdomen and Pelvis

MSAT (Macroscopic Slide Agglutination Test)

MAT (Microscopic Agglutination Test)

Diagnosis: Uncomplicated Leptospirosis / complicated Leptospirosis

Treatment:

Oral Doxycycline / I.V. Penicillin (in severe cases with organ dysfunctions)

IV fluids, Antipyretics

Supportive treatment

Outcome

Ref.No. /ME1/2007

Stanley Medical College,
Chennai-1 Dt. -9-2007

Sub:Medical Education–Stanley Medical College, Chennai–
Ethical Committee constituted for approval of Dissertation/
Thesis submitted–regarding.

The Ethical Committee meeting was held on 3-9-2007 and 7-9-2007 to discuss the paper submitted for Dissertation /Thesis.

The following Members of the Ethical Committee were present and discuss in detail for the approval of the papers presented by the individual by means of power point presentation.

Dr.A.Sundaram, Dean incharge,
Dr.S.Madhavan, Prof. of Pharmacology,
Dr.Thenmozhivalli, Prof. of Microbiology,
Dr.S.Natarajan, Prof. of Medicine,
Dr.K.Balasubramanian, Prof. of Physiology
Dr.M.L.Shyamala, Prof. of Surgery,
Thiru M.Panneerselvam, Junior Administrative Officer.

LIST OF PAPERS SUBMITTED FOR ETHICAL COMMITTEE APPROVAL
ETHICAL MEETING

Dr. Kiruba Mohan, Prof. of Dermatology

1."N.O.C. for PMS study of pregabalin" - Dr.Parimalam Kumar
2. " A Phase IIb/III trial of LLL-3348 of lupin ltd in plaque psoriasis - Dr.A.Ramesh

Dr.M.Thirunavkarasu, M.D.(Psy)D.PM , Prof. of Psychiatry

"Prevalence, socio-demographic variables and method of suicide among various causes of death."

(2)Psychological autopsy of suicide.

V.Rohit

Effect of chewing gums (XYLITOL)

K.Chinthnidhi

Mycotic infections in immuno compromised and cancer patients.

Malavika Prasad

Profile of Hypertensive emergencies - A study of 100 cases from Dept. of medicine, GSH.

3. Sandhya Rani.C Final MBBS,

Assessment of coverage and quality of maternal and child health services at Minjur Primary Health Centre; Block level

4.C.Muralidharan, Final year.

The implications of mobile phones on hearing loss.

5.V.Sarath Chander, 3rd MBBS

Prevalence of Deafness in children.

6.B.Madhusoothanan, 3rd year

(1) Lung functions in type 2 diabetes.

(2)Hyponatremia in intensive medical care patients in GSH.

7.S.Sathyapriya – II MBBS.,

"A study about screening tests for cases of urinary tract infections (UTIs)Using Urine samples."

8.S.Moogaambiga,

"Estended spectrum beta lactamase producing microbes.

POST GRADUATES

1.Dr.R.Arunprakas –M1. P.G.

Analysis of clinical profile of systemic lupus erythematosus

2.Dr.S.Murugananth – M.2 P.G.

Clinical Profile of infectious fevers

3.Dr.N.Loganathan – M2 P.G.

Clinical and Epidemiological profile of Human Leptospirosis in North Chennai.

4.Dr. K. Babu – M3 – P.G.

Study of Clinical Profile of patients with acute inferior wall myocardial infarction.

5.Dr. S.P.Maharajan – M3 – P.G.

Analytical study of atrial fibrillation in Govt. Stanley Medical College Hospital.

6.Dr.P.R.Sowmini – M3 - P.G.

Clinical profile of arrhythmias complicating acute anterior wall myocardial infarction.

7.Dr.E.Uma Maheswari – M4 – PG

Clinical Radiological analysis of Focal seizures with CT Scan.

8.Dr.S.Sudha Selvi, M4 - PG

Clinical profile of chronic obstructive pulmonary disease.

9.Dr.N.Jayanthi. M6- PG

Prevalence of B2 glycoprotein 1 Dependent anticardiolipin antibodies in acute ischemic stroke.

10.Dr.Lavanya. S. – MD PG

Comparative study of fasting lipid profile in chronic renal failure patients on conservative management, on dialysis and after renal transplant.

11.Dr.R.Geetha – Pharmacology

Evaluation of the sedative effects produced by antihistamines inhealthy volunteers by new techniques.

12.Dr.K.G.Devibala, Pharmacology

To evaluate the efficacy of rupatadine in controlling pruritis in lichen planus.

13.Dr.B.Anitha, Physiology

Visual Evoked potentials in hypothyroid patients.

14.Dr.M.Thirumaran, Physiology

Heart rate variability analysis in alcohol dependant individuals.

15.Dr.K.Vinod, Anaesthesia

Real time ultra sound guided catheterization of IJV – A prospective comparison with land mark guided technique.

16.Dr.Rajesh. C.P. – M6 – PG

Cardiac conduction abnormalities and asymptomatic myocardial infarction in NIDDM patients.

The papers presented to the Committee members by the Profs./Asst. Prof./Post Graduates/Under graduates were discussed across the table while their presentation.

The above papers discussed in detail with its supportive documents submitted by them and approved the above papers submitted for Ethical Committee.

Name of the Members	Signature
Dr.A.Sundaram, Dean incharge,	
Dr.S.Madhavan, Prof. of Pharmacology,	8/10/07.
Dr.Thenmozhivalli, Prof. of Microbiology,	
Dr.S.Natarajan, Prof. of Medicine,	9.10.2007.
Dr.K.Balasubramanian, Prof. of Physiology,	
Dr.M.L.Shyamala, Prof. of Surgery,	08/10/07
Thiru M.Panneerselvam, Junior Administrative Officer.	

CHENNAI CITY MAP